UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

Date: September 13, 2005

MEMORANDUM

SUBJECT: **Dicamba:** HED Chapter of the Reregistration Eligibility Decision Document (RED) - Phase I. PC Code: 029801; DP Barcode: D317720.

Regulatory Action: Phase 1 Reregistration Action
Risk Assessment Type: Single Chemical Aggregate

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SEP 28 2005

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1.0 Executive Summary

Dicamba (2-methoxy-3,6-dichlorobenzoic acid) is a selective benzoic acid herbicide registered for the control of certain broadleaf weeds and woody plants before their emergence. It is an auxin agonist that is readily translocated symplastically and apoplastically with accumulation in meristemic regions of the plant. Sensitive plants exhibit rapid uncontrolled growth characterized by twisting and curling of stems and petioles, stem elongation and swelling and leaf cupping. Weed control is generally achieved in 5 to 7 days.

Different forms of dicamba (acid and salt) have registered uses on rights of way areas, asparagus, barley, corn (field and pop), grasses grown in pasture and rangeland, oats, proso millet, rye, sorghum, soybeans, sugarcane, and wheat. Application rates range from 0.5 to 2.8 lb ae/A. Residential uses include broadcast and spot treatment on golf courses and lawns.

Dicamba has a low acute toxicity via oral, dermal or inhalation route. It is an eye and dermal irritant but it is not a skin sensitizer. Following oral administration, dicamba is rapidly absorbed and excreted in urine and feces. Consistent neurotoxic signs (e.g., ataxia, decreased motor activity, impaired righting reflex and gait) were observed in many studies in rats and rabbits at high doses. There was an increased incidence of abortion in the rabbit developmental toxicity study at doses that also showed maternal toxicity. In a two-generation reproduction study, offspring toxicity was manifested as decreased pup body weight gain in all generations at a dose lower than the parental systemic toxicity NOAEL. Developmental studies in rats and rabbits showed no evidence (qualitative or quantitative) for increased susceptibility following *in utero* and/or pre-/post-natal exposure of dicamba. Dicamba is classified as **"Not Likely to be Carcinogenic to Humans"** by the oral route. Mutagenicity studies did not demonstrate evidence of mutagenic potential for dicamba although some positive results were reported in published literature.

An acute neurotoxicity study in rats was selected for the general population, including infants and children, for an endpoint of concern for a single oral exposure risk assessment. For the short- and intermediate-term incidental oral exposure and the chronic RfD, a multi-generation reproduction study in rats was selected based on impaired pup growth (decreased pup weights).

The dermal exposure limits for all durations were based on a multi-generation reproduction study in rats. The rat 28-day dermal toxicity study was not selected because the offspring effect in the reproductive study was not measured in this study. In addition, the NOAEL (1000 mg/kg/day) in the 28-day dermal toxicity study would not be protective of the reproductive-offspring effects in the rat multi-generation reproduction study with a NOAEL of 45 mg/kg/day using a dermal absorption factor of 15%. The multi-generation reproduction study with a longer duration and a NOAEL of 45 mg/kg/day will be protective and appropriate for short-, intermediate- and long-term dermal risk assessments. Since an oral NOAEL was selected, a 15% dermal absorption factor was used for route-to-route extrapolation for assessing dermal risk.

The inhalation endpoints selected paralleled the determinations made for the dermal exposure assessments above and assumed a 100% default assumption in the absence of a repeated exposure inhalation toxicity study.

The uncertainty factors used in determining the acute and chronic RfD exposure limit were 100x (10x for intraspecies variation and 10x for interspecies extrapolation). An additional 3x was applied to acute dietary risk assessment for general population for using a LOAEL in establishing the acute reference dose.

Several plant metabolism studies have been submitted for dicamba. Generally there are two major plant metabolites 3,6-dichloro-5-hydroxybenzoic acid (5-OH dicamba) and 3,6-dichlorosalicylic acid (DCSA), which are structurally similar to the parent compound and are included in the dietary risk assessment. The dietary exposure estimates were conducted assuming 100% crop treated and tolerance-level residues in all crops. For the acute and chronic assessments the most highly exposed subgroup was children, ages 1-2. The exposure estimates were well below the levels of concern, with the acute exposure at 5.4% of the acute population adjusted dose (aPAD) and the chronic exposure at 6.5% of the chronic population adjusted dose (cPAD). The actual exposures are likely to be much lower than those estimated in this assessment because of the percent crop treated and residue levels used in this evaluation.

Dicamba could potentially be found in drinking water. Environmental fate studies show that the major environmental degradate would be DCSA. Sufficient drinking water monitoring data from surface water sources were not available so estimated drinking water concentrations (EDWCs) were determined for surface water resources using PRZM-EXAMS. Ground water monitoring data were used for a scoping assessment when ground water could be a source of drinking water. When food and water exposures are aggregated the total dietary exposure for acute and chronic scenarios are well below the level of concern for all population groups.

Exposure to dicamba may occur in residential settings from treatment of turf around the home and at golf courses. Residential handler assessments were conducted for homeowners applying dicamba to lawns using various types of application equipment. Residential post-application assessments were conducted for adults doing yardwork after application or playing golf on treated turf, and were conducted for children playing on a treated lawn or consuming dirt or pesticide granules while playing. Even when exposures occur on the day of treatment, all of the residential exposures are considerably below the level of concern.

The Food Quality Protection Act (FQPA) requires EPA to aggregate or add exposures from food, water, and residential settings. When residential handler or post-application exposures are added to food and water exposures for any exposure duration, the risk estimates are all well below the levels of concern. For example, the scenario with the highest exposure estimate, a child playing on a treated lawn and consuming treated food) produced a margin of exposure (MOE) of 1030; any exposure with an MOE exceeding 100 is considered to be not of concern.

The risks for occupational exposures were estimated for pesticide applicators as well as people who may enter treated fields after application. The MOEs were calculated for short/intermediate term dermal and inhalation exposures using standard assumptions and unit exposure data for a wide range of application methods and equipment. The unit exposure data were taken from the Pesticide Handlers Exposure Database (PHED) and the Outdoor Residential Exposure Task Force (ORETF) studies for professional lawn care operators. All of the mixer/loader MOEs exceed the target of 100 with the single layer personal protective equipment (PPE) and are not of

concern. The MOEs for applicators are above 100 with baseline or single layer PPE . The MOEs for the mixer/loader/applicators are acceptable with single layer PPE and the MOEs for the flaggers are acceptable with baseline PPE. The labels typically require baseline clothing with water proof gloves. There are no residual concerns regarding occupational exposure to dicamba.

2.0 Ingredient Profile

2.1 Summary of Registered/Proposed Uses

Dicamba (2-methoxy-3,6-dichlorobenzoic acid) is a selective benzoic acid herbicide registered for the control of certain broadleaf weeds and woody plants before their emergence. It is an auxin agonist that is readily translocated symplastically and apoplastically with accumulation in meristemic regions of the plant. Sensitive plants exhibit rapid uncontrolled growth characterized by twisting and curling of stems and petioles, stem elongation and swelling and leaf cupping. Weed control is generally achieved in 5 to 7 days.

Different forms of dicamba (acid and salt) have registered uses on rights of way areas, asparagus, barley, corn (field and pop), grasses grown in pasture and rangeland, oats, proso millet, rye, sorghum, soybeans, sugarcane, and wheat. Application rates range from 0.5 to 2.8 lb ae/A. Residential uses include broadcast and spot treatment on golf courses and lawns.

The registrants intend to support all currently registered uses described in the Use Profile, which is provided in Appendix B of this document. The different forms of dicamba acid and salts that will be supported for reregistration, include: the dicamba acid (PC Code 029801), dimethylamine (DMA) salt (PC Code 029802), sodium (Na) salt (PC Code 029806), isopropylamine (IPA) salt (PC Code 128944), diglycolamine (DGA) salt (PC Code 128931), and potassium (K) salt (PC Code 129043).

There were approximately 434 active products of Dicamba formulated from 6 different forms. The acid, dimethylamine and sodium salt ester forms of Dicamba have the most products. The products are formulated as liquids, standard granules and water dispersible granules. The residential products are typically formulated as granular weed and feed formulations or as liquids in concentrates or ready to use sprays.

2.2 Structure and Nomenclature

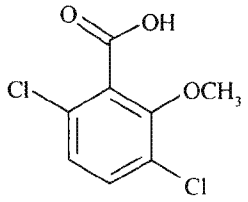
TABLE 2.1. Dicamba and its Salts Nomenclature	
PC Code 029801	
Chemical structure	

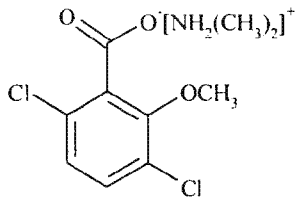
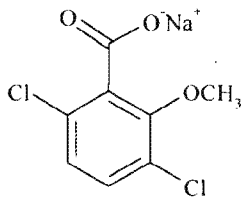
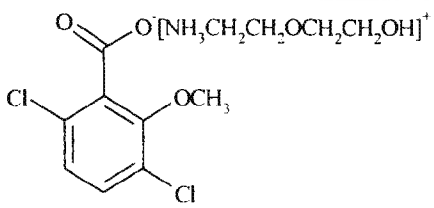
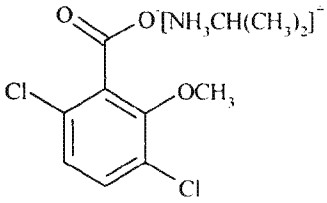
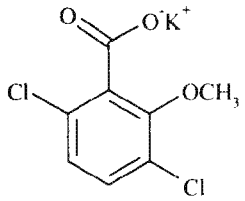
TABLE 2.1. Dicamba and its Salts Nomenclature	
Common name	Dicamba acid
Molecular Formula	$C_8H_6Cl_2O_3$
Molecular Weight	221.04
IUPAC name	3,6-dichloro-*o*-anisic acid
CAS name	3,6-dichloro-2-methoxybenzoic acid or 2-methoxy-3,6-dichlorobenzoic acid
CAS #	1918-00-9
PC Code 029802	
Chemical structure	
Common name	Dicamba dimethylamine salt (DMA salt)
Molecular Formula	$C_{10}H_{13}Cl_2NO_3$
Molecular Weight	266.1
CAS #	2300-66-5
PC Code 029806	
Chemical structure	
Common name	Dicamba sodium salt (Na salt)
Molecular Formula	$C_8H_5Cl_2NaO_3$
Molecular Weight	243.0
CAS #	1982-69-0
PC Code 128931	
Chemical structure	
Common name	Dicamba diglycolamine salt (DGA salt)
Molecular Formula	$C_{12}H_{17}Cl_2NO_5$
Molecular Weight	326.18
CAS #	104040-79-1
PC Code 128944	

TABLE 2.1. Dicamba and its Salts Nomenclature	
Chemical structure	
Common name	Dicamba isopropylamine salt (IPA salt)
Molecular Formula	$C_{11}H_{15}Cl_2NO_3$
Molecular Weight	280.15
CAS #	55871-02-8
PC Code 129043	
Chemical structure	
Common name	Dicamba potassium salt (K salt)
Molecular Formula	$C_8H_5Cl_2KO_3$
Molecular Weight	259.1
CAS #	10007-85-9

2.3 Physical and Chemical Properties

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Dicamba acid (PC Code 029801)		
Melting point	114-116 °C (PAI) 90-100 °C (87% TGAI)	SRR Reregistration Standard, 6/30/89
pH	2.5-3.0 (87% TGAI)	
Density, bulk density, or specific gravity	1.57 g/mL at 25 °C (87% TGAI)	
Water solubility	0.5 g/100 mL at 25 °C (PAI)	
Solvent solubility	g/100 mL at 25 °C (PAI) dioxane 118.0 ethanol 92.2 isopropyl alcohol 76.0 methylene chloride 26.0 acetone 17.0 toluene 13.0 xylene 7.8 heavy aromatic naphthalene 5.2	

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Vapor pressure	3.4 x 10^{-5} mm Hg at 25 °C (PAI)	
Dissociation constant, pK_a	1.97 (PAI)	
Octanol/water partition coefficient	0.1 (PAI)	
UV/visible absorption spectrum	neutral: 511 (275 nm) acidic (pH 0-1): 1053 (281 nm) basic (pH 13-14): 469 (274 nm)	RD D266167, 6/26/00, B. Kitchens
Dicamba DMA salt (PC Code 029802)		
Melting point	101.0-114.5 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	3.89 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.77 g/mL at 25 °C (tap density)	
Water solubility	94.5 g/100 mL at 25 °C	
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	D198000, 5/5/94, P. Deschamp
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	K_{ow} = 0.078	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
UV/visible absorption spectrum	**Not available**	
Dicamba Na salt (PC Code 029806)		
Melting point	320-325 °C	RD Memorandum, 9/26/94, T. Alston
pH	7.16	
Density, bulk density, or specific gravity	1.03 g/mL at 25 °C	
Water solubility	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the Na salt	D198000, 5/5/94, P. Deschamp
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the Na salt	
UV/visible absorption spectrum	**Not available**	
Dicamba DGA salt (PC Code 128931)		

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Melting point	52.0-85.0 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	7.60 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.69 g/mL at 25 °C (tap density)	
Water solubility	107 g/100 mL at 25 °C	
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	D198000, 5/5/94, P. Deschamp
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	K_{ow} = 0.061	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
UV/visible absorption spectrum	Not available	
Dicamba IPA salt (PC Code 128944)		
Melting point	93.5-127.5 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	4.68 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.63 g/mL at 25 °C (tap density)	
Water solubility	59.6 g/100 mL at 25 °C	
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	D198000, 5/5/94, P. Deschamp
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	K_{ow} = 0.070	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
UV/visible absorption spectrum	Not available	
Dicamba K salt (PC Code 129043)		
Melting point	Decomposes at 213.5 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	8.12 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.88 g/mL at 25 °C (tap density)	
Water solubility	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the K salt	D198000, 5/5/94, P. Deschamp
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	
Vapor pressure		

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Dissociation constant, pK_a		
Octanol/water partition coefficient	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the K salt	
UV/visible absorption spectrum	**Not available**	

3.0 Hazard Characterization/Assessment

3.1 Hazard and Dose-Response Characterization

Dicamba has a low acute toxicity via oral, dermal or inhalation route. It is an eye and dermal irritant but it is not a skin sensitizer. Following oral administration, dicamba is rapidly absorbed and excreted in urine and feces without significant metabolism. Dogs are generally considered to be toxicologically more sensitive when exposed to dicamba. However, a submitted toxicity study in dogs showed that no effect was seen at the highest dose tested (52 mg/kg/day) which indicated that the animals in the study were not tested at high enough doses. Consistent neurotoxic signs (e.g., ataxia, decreased motor activity, impaired righting reflex and gait) were observed in many studies in rats and rabbits at high doses. There is an increased incidence of abortion in the rabbit developmental toxicity study at doses that also showed maternal toxicity. In a two-generation reproduction study, offspring toxicity was manifested as decreases in pup weight in all generations at a dose lower than the parental systemic toxicity NOAEL. Developmental studies in rats and rabbits showed no evidence (qualitative or quantitative) for increased susceptibility following *in utero* and/or pre-/post-natal exposure of dicamba. Dicamba is classified as **"Not Likely to be Carcinogenic to Humans"** by the oral route. Mutagenicity studies did not demonstrate evidence of mutagenic potential for dicamba although some positive results were reported in published literature.

An acute-neurotoxicity study in rats was selected for the general population, including infants and children, for an endpoint of concern for a single oral exposure risk assessment. For the short- and intermediate-term incidental oral exposure and the chronic RfD, a multi-generation reproduction study in rats was selected based on impaired pup growth (decreased pup weights).

The dermal exposure limits for all durations were based on a multi-generation reproduction study in rats. The rat 28-day dermal toxicity study was not selected because the offspring effect in the reproductive study was not measured in this study. In addition, the NOAEL (1000 mg/kg/day) in the 28-day dermal toxicity study would not be protective of the reproductive-offspring effects in the rat multi-generation reproduction study with a NOAEL of 45 mg/kg/day using a dermal absorption factor of 15%. The multi-generation reproduction study with a longer duration and a NOAEL of 45 mg/kg/day will be protective and appropriate for short-, intermediate- and long-term dermal risk assessments. Since an oral NOAEL was selected, a 15% dermal absorption factor was used for route-to-route extrapolation.

The inhalation endpoints selected paralleled the determinations made for the dermal exposure assessments above and assumed a 100% default relative inhalation to oral absorption assumption in the absence of a repeated exposure inhalation toxicity study.

The uncertainty factors used in determining the acute and chronic RfD exposure limit were 100x (10x for intraspecies variation and 10x for interspecies extrapolation). An additional 3x was applied to acute dietary risk assessment for general population for using a LOAEL because most of the clinical signs of neurotoxicity were seen at repeated doses of 150 mg/kg/day or above (TXR No. 0050280).

Note that a profile of the acute toxicity studies may be found in Table 3.1 and other studies may be found in Table 3.2.

3.2 Absorption, Distribution, Metabolism, Excretion (ADME)

Multiple studies describing the metabolism or the pharmacokinetic of dicamba in rats have been submitted to the Agency. The metabolism study in rats showed that following oral administration, dicamba is rapidly absorbed and excreted. Over 95% is excreted in the urine and the compound is not metabolized or accumulated by the tissues.

The plasma pharmacokinetic studies in rats showed that absorption of the radiolabeled dicamba was rapid, with peak plasma concentrations found within 2 hours of treatment. Absorption was not saturated, even at the highest dose, as indicated by increasing plasma concentrations with doses. However, the increase in plasma concentration was non-linear and disproportionate from one dose to the next doses, which is consistent with saturation of excretion. No significant treatment-related differences between the sexes or time of radiolabel administration were found. Another plasma pharmacokinetic study suggested that dicamba acts as an inhibitor of renal anion transport.

Table 3.1. Acute Toxicity Profile on Dicamba

OPPTS Guideline	Study Type	MRID	Results	Toxicity Category
870.1100	Acute oral toxicity / rat	00078444	LD_{50} => 2740 mg/kg	III
870.1200	Acute dermal toxicity / rat	00241584	LD_{50} => 2000 mg/kg	III
870.1300	Acute inhalation toxicity / rat	00263861	LC_{50} => 5.3 mg/L	IV
870.2400	Primary eye irritation / rabbit	00241584	Irritant	II

Table 3.1. Acute Toxicity Profile on Dicamba				
870.2500	Primary dermal irritation / rabbit	00237955	Irritant	II
870.2600	Dermal sensitization / guinea pig	00263861	Non-Sensitizer	--

Table 3.2. Subchronic, Chronic and Other Toxicity Profile for Dicamba		
Guideline No./ Study Type/	**MRID Nos. Doses/Classification**	**Results**
870.3100 Subchronic Oral - Rat	44623101 (1997) (0, 500, 3000, 6000, 12000 ppm) M:0,40.1,238.7,479.4,1000 mg/kg/day F:0,43.2,266.4,535.6,1065.3 mg/kg/day Acceptable/Guideline	NOAEL= 479.4/535.6 mg/kg/day(M/F). LOAEL= 1000/1065.3 mg/kg/day (M/F) based on clinical signs, decr. body weight gains, incr. liver wt and incr. centrolobular hepatocyte hypertrophy and hepatocellular pigmentation.
870.3200 28-Day dermal toxicity - Rat	45814501 (2002) 0,30,300,1000 mg/kg/day (M/F) Acceptable/Guideline	NOAEL= 1000 mg/kg/day (HDT) LOAEL= not determined.
870.3700a Prenatal developmental - Rat	00084024 (1981) 0,64,160,400 mg/kg/day (GD 6-19) Acceptable/Guideline	**Maternal**: NOAEL= 160 mg/kg/day; LOAEL= 400 mg/kg/day based on Incr. mortality, clinical signs, decr. body weight gains, decr. food consumption. **Developmental**: NOAEL= 400 mg/kg/day (HDT), LOAEL not established.
870.3700b Prenatal developmental - NZW Rabbit	42429401 (1992) 0,30,150,300 mg/kg/day (GD 6-18) Range-finding: 0,62.5,125,250,500 mg/kg/day (GD 6-18) Acceptable/Guideline	**Maternal**: NOAEL= 62.5 mg/kg/day, LOAEL= 150 mg/kg/day based on incr. abortion, clinical signs (decr. motor activity, ataxia). **Developmental**: NOAEL= 62.5 mg/kg/day, LOAEL= 150 mg/kg/day based on incr. abortion.
870.3800 Reproduction and fertility effects - Rat	43137101 (1993) (0,500,1500,5000 ppm) M: 0,40,122,419 mg/kg/day F: 0,45, 136, 450 mg/kg/day Acceptable/Guideline	**Parental/Systemic:** NOAEL= 122/136 mg/kg/day (M/F); LOAEL= 419/450 mg/kg/day (M/F) based on clinical signs (slow righting reflex). **Reproductive:** NOAEL=122 mg/kg/day; LOAEL= 419 mg/kg/day based on delayed sexual maturation in F1 males. **Offspring:** NOAEL=45 mg/kg/day; LOAEL= 136 mg/kg/day based on impaired pup growth (decr. pup weights) in all generations during lactation period.
870.4200a Chronic Toxicity/ Carcinogenicity -Rat	00146150 (1985) (0,50,250,2500 ppm) M: 0,2,11,107 mg/kg/day F: 0,3,13,127 mg/kg/day Acceptable/Guideline	NOAEL= 107/127 mg/kg/day (M/F), LOAEL was not established. Not carcinogenic. The study is considered adequate for evaluating the carcinogenic potential.

Table 3.2. Subchronic, Chronic and Other Toxicity Profile for Dicamba		
Guideline No./ Study Type/	**MRID Nos. Doses/Classification**	**Results**
870.4100b Chronic toxicity - dog	40321102 (1986) (0,100,500,2500 ppm) 0,2,11,52 mg/kg/day Acceptable/Guideline	NOAEL=52 mg/kg/day (HDT).
870.4200b Carcinogenicity - mouse	40872401 (1988) (0,50,150,1000,3000 ppm) M: 0,5.5,17.2,108,358 mg/kg/day F: 0,5.8,18.8,121,354 mg/kg/day Acceptable/Guideline	NOAEL=358/354 mg/kg/day (M/F), LOAEL was not established. Not carcinogenic. The study is considered adequate for evaluating the carcinogenic potential.
870.5100 Gene Mutation Salmonella typhimurium	00143001(1979) Acceptable/Guideline	Not mutagenic.
870.5395 Chromosome aberration (CHO)	40321101 (1986) Acceptable/Guideline	Chromosome aberrations were not induced in a cultured CHO cells at concentrations of 2330, 1170, 590, and 300 µg/mL either with or without S-9 activation.
870.5550 Unscheduled DNA synthesis (UDS)	00143001 (1979) Acceptable/Guideline	No evidence of UDS at levels 0.1 to 3000 µg/mL.
870.6200 Acute Neurotoxicity - Rat	42774104 (1993) 0,300,600,1200 mg/kg Acceptable/Guideline	NOAEL was not established, LOAEL=300 mg/kg based on severe neurologic signs (impaired respiration, rigidity upon handling, prodding, or dropping, impaired gait and righting reflex in both sexes.
870.6200 Subchronic neurotoxicity - Rat	43245210 (1994) (0,3000,6000,12000 ppm) M:0,197.1,401.4,767.9 mg/kg/day F: 0,253.4,472.0,1028.9 mg/kg/day Acceptable/Guideline	NOAEL= 401.4/472.0 mg/kg/day (M/F); LOAEL= 767.9/1028.9 mg/kg/day (M/F) based on rigidity body tone, slightly impaired righting reflex and gait.
870.6300 Developmental Neurotoxicity -Rat	Data Gap	Not available.
870.7485 Metabolism	00028261(1967) Acceptable/guideline	Rapidly absorbed and excreted in urine and feces. Dicamba is not metabolized or bioaccumulation.

3.3 FQPA Considerations

The database is adequate in terms of endpoint studies and dose response information to select appropriate endpoints for prenatal or postnatal risk for infants and children. There is no evidence (qualitative or quantitative) of increased susceptibility following *in utero* and/or pre-natal exposure in the developmental toxicity studies in rats and rabbits. There was evidence of increased sensitivity to the offspring following pre- and/or postnatal exposure in the two-generation reproduction study in rats. In that study, offspring toxicity was manifested as decreased pup body weight in all generations at a dose lower than the parental systemic toxicity NOAEL. However, the degree of concern is low for the quantitative susceptibility because the risk assessment was based on the very same effect seen in the pups with a definitive NOAEL. There are no concern or residual uncertainties for pre- and postnatal toxicity.

After considering the available toxicity data, the risk assessment team determined that a developmental neurotoxicity study (DNT) is not required based on the following reasons: (1) although clinical signs of neurotoxicity were seen in pregnant animals, no evidence of developmental anomalies of the fetal nervous system were observed in the prenatal developmental toxicity studies, in either rats or rabbits, at maternally toxic doses up to 300 or 400 mg/kg/day, respectively; (2) there were no evidence of behavioral or neurological effects on the offspring in the two-generation reproduction study in rats; (3) the ventricular dilation of the brain in the chronic toxicity study was only observed in females at the high dose after two years exposure. The significance of this observation is questionable since no similar histopathological finding was seen in the subchronic neurotoxicity study. In addition, the dicamba risk assessment team evaluated the quality of the exposure data; and, based on these data, recommended that the special FQPA SF be reduced to 1x.

3.3.1 Adequacy of the Toxicity Data Base

The following studies are available in the toxicity database:

- Developmental toxicity studies in rats and rabbits (acceptable).
- Two generation reproduction study in rats (acceptable).
- Acute and subchronic neurotoxicity studies in rats (acceptable).

3.3.2 Evidence of Neurotoxicity

There is evidence of neurotoxicity resulting from exposure to dicamba. The velevant findings are summarized below and the executive summaries of studies are presented in Appendix A.

In the acute neurotoxicity study, at 300 mg/kg bw or above, clinical signes of neurotoxicity consisted of impaired gait and righting reflex, decreased arousal and rears/minutes, and rigidity upon handling were found. At higher dose levels, the effects were more pronounced with additional effects. The subchronic neurotoxicity study in rats showed rigid body tone, impaired righting reflex and gait at 768 mg/kg.

In the developmental toxicity studies in rats ataxia, stiffening of the body when touched, and decreased motor activity were seen at 400 mg/kg in the dams. The developmental toxicity study in rabbits showed that at 150 mg/kg the dams presented signs of ataxia, rales and decreased motor

activity.

A two generation reproduction study demonstrated tense/stiff body tone and slow righting reflex in the dams from both generations at approximately 450 mg/kg. It should be noted that the signs of neurotoxicity were consistent across several studies.

3.3.3 Developmental Toxicity Studies

In a developmental toxicity study (MRID No. 00084024), pregnant (CD Charles River) rats (25/dose group) received gavage administration of dicamba (85.3%) in corn oil at dose levels of 0, 64, 160, or 400 mg/kg/day during gestation days 6 through 19. Maternal toxicity limited to the high dose (400 mg/kg/day) was characterized by mortality in three gravid and one non-gravid dams that exhibited neurotoxic signs prior to death; clinical signs of nervous system toxicity that included ataxia, salivation, stiffening of the body when held, and decreased motor activity; statistically significant ($p<0.05$) decreases in body weight gain during the dosing period; and concomitant decreases in food consumption. Dicamba had no effect on any of the cesarean parameters. For maternal toxicity, the NOAEL was 160 mg/kg/day and the LOAEL was 400 mg/kg/day based on mortality, clinical signs, body weight changes and decreases in food consumption. No Treatment-related fetal gross external, skeletal or visceral anomalies (malformations or variations) were seen at any dose level. For developmental toxicity, the NOAEL was >400 mg/kg/day; a LOAEL was not established. This study is classified **acceptable/guideline** (OPPTS 870.3700a) and satisfies the requirements for a developmental toxicity study in the rat.

In a developmental toxicity study (MRID No. 42429401), inseminated New Zealand White rabbit (19-20/dose) were given oral capsules containing dicamba (90.5%) at dose levels of 0, 30, 150, or 300 mg/kg/day from days 6 through 18 of gestation. No maternal or developmental toxicity was observed at 30 mg/kg/day. At 150 mg/kg/day, maternal toxicity was characterized by abortion (5%) and clinical signs such as ataxia, rales, decreased motor activity. At 300 mg/kg/day maternal toxicity was manifested by abortions (20%), clinical signs, decreased body weight and body weight gain and food consumption. Developmental toxicity at 300 mg/kg/day was manifested by irregular ossification of the nasal bones of the skull. At 150 mg/kg/day, increased incidence of abortion was observed and was considered developmental toxicity. In a range-finding study, NZW rabbits were dosed at 0, 62.5, 125, 250, or 500 mg/kg/day from days 6 through 18 of gestation. No maternal or developmental toxicity was observed at 62.5 mg/kg/day. Treatment-related maternal toxicity was manifested by mortality, increased resorptions and reduction in the litter size at 500 mg/kg/day. Clinical signs occurred at 125, 250, and 500 mg/kg/day. Cesarean sections revealed no treatment-related differences between treated and control groups, and no external malformation or variations were seen in any of the fetuses of the treated does. Based on the results of these studies, the NOAEL for maternal toxicity was 62.5 mg/kg/day and the LOAEL was 150 mg/kg/day based on increased incidences of abortion and clinical signs (i.e., decreased motor activity, ataxia). For developmental toxicity, the NOAEL was 62.5 mg/kg/day and the LOAEL was 150 mg/kg/day based on increased incidence of abortion. This study is classified **acceptable/guideline** (OPPTS 870.3700b; OECD 414) and satisfies the requirements for a developmental toxicity study in the rabbit.

3.3.4 Reproductive Toxicity Study

In a two-generation reproduction study (MRID 43137101), Sprague-Dawley rats (32 or 28/group) received dicamba technical (86.5%) in the diet at dose levels of 0, 500, 1500, or 5000 ppm (0, 40, 122, or 419 mg/kg/day for males and 0, 45, 136 or 450 mg/kg/day for females, respectively) for two generations. Systemic toxicity was observed at 5000 ppm, manifested as clinical signs in dams from both generations during lactation (tense/stiff body tone and slow righting reflex) and significantly increased relative liver to body weights (112% of control) in both generations and sexes, adults as well as weanlings. The increase (107%) in relative kidney weights observed at 1500 and/or 5000 ppm were not considered to be toxicologically significant due to lack of corroborative gross or histopathological lesions in the kidneys. Sexual maturation among male pups in the F1 generation was significantly delayed at 5000 ppm. Similar effects were not seen in females. Significantly decreased pup body weights were observed in all generations and matings at 1500 ppm (86 - 90% of control) and at 5000 ppm (74 - 94% of control) throughout lactation. For parental systemic toxicity, the NOAEL was 122 and 136 mg/kg/day for males and females, respectively, and the LOAEL was 419 and 450 mg/kg/day in males and females based on clinical signs of neurotoxicity. For reproductive toxicity, the NOAEL was 122 mg/kg/day and the LOAEL was 419 mg/kg/day based on delayed sexual maturation in F_1 males. For offspring toxicity, the NOAEL was 45 mg/kg/day and the LOAEL was 136 mg/kg/day based on decreased pup body weight. This study is classified as **acceptable/guideline** and satisfies the guideline requirements (OPPTS 870.3800; OECD 416) for a two-generation reproduction study in the rat.

3.3.5 Additional Information from Literature Sources

No additional relevant toxicity studies from published literature were identified.

3.3.6 Pre-and/or Postnatal Toxicity

3.3.6.1 Determination of Susceptibility

There is no evidence of increased qualitative or quantitative susceptibility following *in utero* and/or pre-natal exposure in the developmental toxicities in rats and rabbits. There was evidence of increased quantitative susceptibility to the offspring following pre- and/or postnatal exposure in the two-generation reproduction study in rats. In that study, offspring toxicity was manifested as decreased pup body weight gain in all generations at a dose lower than the parental systemic toxicity NOAEL. However, the NOAEL of 45 mg/kg/day identified in this study was chosen for risk assessments for all routes and exposure durations other than acute oral exposures. Since this NOAEL is the lowest (most sensitive endpoint) in the dicamba toxicity data base, and the dose-response observed in the study is well defined assuring that this dose is a clear NOAEL, use of the NOAEL and endpoint for risk assessment is protective for all observed toxic effects of the chemical. Therefore, there is low concern for the increased susceptibility observed in the reproduction study since all appropriate risk assessments utilize this endpoint. Additionally, there is no increased susceptibility observed in the developmental toxicity studies. Since the most sensitive observed developmental endpoint (increased incidence of abortion) and the associated NOAEL was used for acute dietary risk assessment for females of child-bearing age, the risk assessment is protective for potential acute toxicity to developing fetuses.

3.3.6.2 Degree of Concern Analysis and Residual Uncertainties

The degree of concern is low for the quantitative susceptibility because the risk assessment was based on the most sensitive endpoint with a definitive NOAEL. There are no concern or residual uncertainties for pre- and postnatal toxicity.

3.3.7 Recommendation for a Developmental Neurotoxicity Study

After considering the available toxicity data, the risk assessment team determined that a developmental neurotoxicity study (DNT) is not required based on the following reasons: (1) although clinical signs of neurotoxicity were seen in pregnant animals, no evidence of developmental anomalies of the fetal nervous system were observed in the prenatal developmental toxicity studies, in either rats or rabbits, at maternally toxic doses up to 300 or 400 mg/kg/day, respectively; (2) there were no evidence of behavioral or neurological effects on the offspring in the two-generation reproduction study in rats; (3) the ventricular dilation of the brain in the chronic toxicity study was only observed in females at the high dose after two years exposure. The significance of this observation is questionable since no similar histopathological finding was seen in the subchronic neurotoxicity study.

3.4 Safety Factor for Infants and Children

3.4.1 Adequacy of the Exposure Data Base

The dietary exposure assessment is based on the exaggerated exposure assumptions, that all crops consumed in the U.S. are treated, and that the commodities bear tolerance level residues. The residential exposure assessment assumes maximum label use rate as well as other conservative assumptions. Therefore, the Agency does not believe that exposure to dicamba will be underestimated.

3.4.2 Conclusion

Based on the hazard data, there are no concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity. In addition, the dicamba risk assessment team evaluated the quality of the exposure data and has no residual uncertainties. Therefore, the team has recommended that the special FQPA Safety Factor be reduced to 1x.

3.5 Hazard Identification and Toxicity Endpoint Selection

A summary of the endpoints and doses selected for risk assessment may be found in Table 3.4 at the end of this section.

3.5.1 Acute Reference Dose (aRfD) - Females age 13-49

No study was identified that demonstrated effects to the developing fetus as a result of a single exposure via the oral route. Therefore, this risk assessment is not required.

3.5.2 Acute Reference Dose (aRfD) - General Population

The results of the Acute Neurotoxicity Study (ACN) in Rats (MRID No.: 42774104) were considered for this endpoint. A summary may be found in Appendix A. The effects observed in this study can be attributed to a single dose and is appropriate for all populations. Neurotoxicity was seen in both sexes at the lowest dose tested, 300 mg/kg/day. With the exception of the decrease in forelimb grip strength, which persisted until day 7, the other neurologic signs such as impaired gaits and righting reflex were seen on the day of dosing. A comparison with the rat developmental toxicity study that had similar clinical signs with a NOAEL of 160 mg/kg/day after 10 days of treatment indicates that the NOAEL for the acute neurotoxicity study is unlikely to be more than 3-fold lower than the LOAEL (ACN LOAEL/3 = 100 mg/kg; rat developmental study NOAEL = 160 mg/kg). Therefore, it was determined that an uncertainty factor of 3 for extrapolation of LOAEL to NOAEL was adequate. The total uncertainty factor is 300x, 10x for interspecies extrapolation, 10x for intraspecies variations, and 3x for using a LOAEL. The acute population adjusted dose for the general population is equal to the acute reference dose and is 1.0 mg/kg/day.

3.5.3 Chronic Reference Dose (cRfD)

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was used for establishing the chronic reference dose. The selected dose and endpoints are appropriate for the route and duration of exposure and is protective of the general population. A summary of this study may found in Section 3.3.4. The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL). An uncertainty factor of 100x is to be applied including 10x for interspecies extrapolation and 10x for intraspecies variations. The chronic population adjusted dose (cPAD) is equal to the chronic reference dose and is 0.45 mg/kg/day.

3.5.4 Incidental Oral Exposure (Short and Intermediate Term)

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was selected for this risk assessment. This study is of the appropriate route and duration of exposure, since effects in the pups were seen on lactation day 21 in both F_2 litters and is protective of the population of concern (infants and children). A summary of this study may found in Section 3.3.4. The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL). An uncertainty factor of 100x is to be applied including 10x for interspecies extrapolation and 10x for intraspecies variations. The chronic population adjusted dose (cPAD) is equal to the chronic reference dose and is 0.45 mg/kg/day.

3.5.5 Dermal Absorption

A dermal absorption study is not available. An upper-bound estimate of dermal absorption was estimated using the NOAEL of 1000 mg/kg/day in the 21-day dermal toxicity rabbit study and the LOAEL of 150 mg/kg/day in the rabbit oral developmental study.

$$\frac{150}{1000} \times 100 = 15\ \%\ \text{dermal absorption factor}$$

3.5.6 Dermal Exposure

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was selected for this endpoint. A summary of this study may found in Section 3.3.4. Although a rat 28-day dermal toxicity study was available which showing no systemic toxicity at the highest dose tested of 1000 mg/kg/day, this dermal study did not assess reproductive and offspring effects. Offspring toxicity in the rat oral multi-generation reproduction study was noted below dosages where parental toxicity was evident. In order to be protective of these effects in the absence of any route-specific data, the reproduction study was chosen for all time periods of exposure, including short-term, since effects in the pups were seen on lactation day 21 in both F_2 litters. Since an oral NOAEL was selected, 15% dermal absorption factor should be used for route-to-route extrapolation. The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL).

3.5.7 Inhalation Exposure

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was used for selecting this endpoint. A summary of this study may found in Section 3.3.4. In the absence of a repeated exposure inhalation study, an oral study is employed. Inhalation absorption is assumed to be equivalent to oral (i.e., 100%). The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL).

3.5.8 Level of Concern for Margin of Exposure

The levels of concern for occupational and residential exposures are summarized in Table 3.3. For **Occupational Exposure** a margin of exposure (MOE) MOE of 100 is required for short-, intermediate-, and long-term occupational risk assessments for both dermal and inhalation routes of exposure. The MOEs for dermal and inhalation exposures may be combined for occupational exposure risk assessment because the toxicity endpoints for these routes of exposure are the same. For **Residential Exposure** a margin of exposure (MOE) of 100 is required for short-, intermediate-, and long-term residential risk assessments for both dermal and inhalation routes of exposure, and an MOE of 300 is required for acute exposures.

Table 3.3. Summary of Target Margins of Exposure (MOEs) for Risk Assessment				
Route	**Duration**			
	Acute (1 day)	**Short-Term (1-30 Days)**	**Intermediate-Term (1 - 6 Months)**	**Long-Term (> 6 Months)**
Occupational (Worker) Exposure				
Dermal	NA	100	100	100
Inhalation	NA	100	100	100
Residential (Non-Dietary) Exposure				
Oral	300	100	100	N/A
Dermal	300	100	100	100
Inhalation	300	100	100	100
N/A = Not Applicable				

3.5.9 Recommendation for Aggregate Exposure Risk Assessments

A common toxicological endpoint (decreased pup growth) of concern was identified for the short-, intermediate- and long-term durations via the oral, dermal (oral equivalent) and inhalation (oral equivalent) routes. Therefore, the aggregate exposure risk assessment should include oral, dermal and inhalation routes appropriate to the population of concern.

3.5.10 Classification of Carcinogenic Potential

In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), dicamba is classified as "**Not Likely to be Carcinogenic to Humans**". This was based on negative cancer studies in rats and mice which were tested at adequate dose levels to assess the carcinogenicity of dicamba (TXR No. 0053647). A detailed discussion of the carcinogenicity studies may be found in Appendix A of this document.

Table 3.4 Summary of Toxicology Endpoint Selection for Dicamba			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (General population including infants and children	LOAEL = 300 mg/kg/day UF = **300** **Acute RfD** = 1 mg/kg/day	FQPA SF = 1X **aPAD** = acute RfD / FQPA SF = 1.0 mg/kg/day	**Acute Neurotoxicity Study in Rats** LOAEL = **300** mg/kg/day (LDT) based on clinical signs of neurotoxicity.

Table 3.4 Summary of Toxicology Endpoint Selection for Dicamba

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Chronic Dietary (All populations)	NOAEL= **45** mg/kg/day UF = **100** **Chronic RfD** = 0.45 mg/kg/day	FQPA SF = 1X **cPAD** = chronic RfD / FQPA SF = 0.45 mg/kg/day	**Multi-generation Reproduction Study in Rats** LOAEL=136 mg/kg/day based on impaired pup growth (decreased pup weights).
Short-Term Incidental Oral (1 - 30 Days)	Oral NOAEL= 45 mg/kg/day	**Residential** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Intermediate-Term Incidental Oral (1 - 6 Months)	Oral NOAEL= 45 mg/kg/day	**Residential** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Short-Term Dermal (1 - 30 days)	Oral NOAEL= 45 mg/kg/day (Dermal absorption rate = 15%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Intermediate-Term Dermal (1 - 6 Months)	Oral NOAEL= 45 mg/kg/day (Dermal absorption rate = 15%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Long-Term Dermal (> 6 Months)	Oral NOAEL= 45 mg/kg/day (Dermal absorption rate= 15%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Short-Term Inhalation (1 - 30 days)	Oral NOAEL= 45 mg/kg/day (Inhalation absorption rate= 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Intermediate-Term Inhalation (1 - 6 Months)	Oral NOAEL= 45 mg/kg/day (Inhalation absorption rate= 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section

Table 3.4 Summary of Toxicology Endpoint Selection for Dicamba			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Long-Term Inhalation (>6 Months)	Oral NOAEL= 45 mg/kg/day (Inhalation absorption rate= 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Cancer (Oral, dermal, inhalation)	**Not Likely to be Carcinogenic to human.**		

3.6 Endocrine disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP). While delayed sexual maturation in females was observed in the rat reproduction study, no effects clearly related to endocrine disruption were seen in the toxicity data base.

When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, dicamba may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

4.0 Public Health and Pesticide Epidemiology Data

4.1 Incident Reports

The OPP Incident Data System (IDS), California Department of Pesticide Regulation, National Pesticide Information Center (NPIC), National Institute of Occupational Safety and Health's Sentinel Event Notification System for Occupational Risks (NIOSH SENSOR), and Poison Control Centers

were reviewed for adverse incidents as a result of dicamba exposure. Dicamba is rarely used as a herbicide by itself. Most often it is mixed with other ingredients, particularly other chlorophenoxy herbicides, such as 2,4-D. Consequently, most incidents involving dicamba exposure also involved exposure to other pesticides as well. There were too few reports of ill effects from exposure to Dicamba in the available data bases to draw conclusions about likely effects. Reigart and Roberts (1999) state that dicamba can be moderately irritating to skin and respiratory tract. This is consistent with reported symptoms from Poison Control Centers.

4.2 Other Pesticide Epidemiology Published Literature

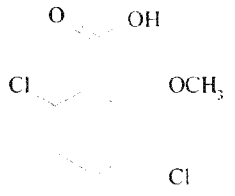
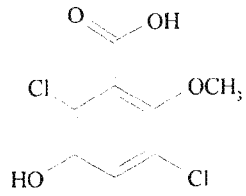
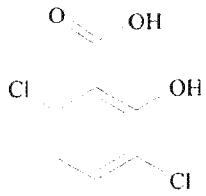
Two epidemiology studies evaluated pesticides and non-Hodgkin's lymphoma (NHL). One study examined residential use and concluded there was "no detectable excess associated with residential exposures" which, for dicamba, were more prevalent in controls than cases. The second study was a multicenter population-based incidence study. In the multivariate model which included exposure to other major pesticides, history of cancer in the case or relatives to the case subject, there was a two-fold risk for dicamba mixtures (odds ratio = 1.96; 95% confidence interval 1.40-2.75) and similar risks were seen for mecoprop and aldrin. The authors concluded that "In our final models, NHL was associated with a personal history of cancer; a history of cancer in first-degree relatives; and exposure to dicamba-containing herbicides, to mecoprop, and to aldrin." The Health Effects Division concludes that this study suggests that dicamba may be associated with NHL, but that the evidence for this association is not strong enough to identify dicamba as a likely or probable cause of NHL. The Agricultural Health Study is planning to assess NHL in the next year; further assessment that will permit a more definitive conclusion concerning dicamba will be available at that time.

5.0 Dietary Exposure/Risk Characterization

5.1 Pesticide Metabolism and Environmental Degradation

5.1.1 Metabolism in Primary Crops

The nature of the residue in plants is adequately understood based on the aggregate of metabolism studies conducted on several crops. The results of these studies indicate that dicamba is rapidly absorbed and translocated by grasses, grapes, black valentine beans, wheat, bluegrass, and soybeans. It is also rapidly absorbed by sugarcane following foliar application but it is very slowly translocated from the leaves to the roots. The metabolism of dicamba in plants proceeds mainly by demethylation and hydroxylation. Major metabolites found include 3,6-dichloro-5-hydroxybenzoic acid (5-OH dicamba) metabolite and 3,6-dichloro-2-hydroxybenzoic acid metabolite, also referred to as 3,6-dichlorosalicylic acid (DCSA). The chemical names and structures of dicamba and its regulated metabolites are depicted below in Table 5.1.

Table 5.1. Chemical names and structures of dicamba and its metabolites.		
		
Dicamba (3,6-dichloro-*o*-anisic acid)	**5-hydroxy dicamba** (3,6-dichloro-5-hydroxy-*o*-anisic acid)	**DCSA** (3,6-dichloro-2-hydroxybenzoic acid or 3,6-dichlorosalicylic acid)

The 8/12/83 Residue Chemistry Chapter of the Dicamba Registration Standard and the 6/30/89 Residue Chemistry Chapter of the Dicamba (SRR) Registration Standard concluded that the major residues found in barley, corn, cotton, grasses, oat, proso millet, sorghum, sugarcane, and wheat are dicamba and its 3,6-dichloro-5-hydroxybenzoic acid (5-OH dicamba) metabolite. It also concluded that in asparagus, the residues of concern are dicamba and DCSA and in aspirated grain fractions and soybeans the residues of concern are dicamba, 5-OH dicamba, and DCSA.

No new data are available or required. HED concludes that these residues are appropriate for the tolerance expression and risk assessment.

5.1.2 Metabolism in Rotational Crops

The nature of the residue in rotational crops is understood. The results of an acceptable confined rotational crop study showed that at a plantback interval of 120 days, the total radioactive residues were <0.01 ppm in/on samples of collard greens (a representative of leafy vegetables) and carrots (a representative of root crops) but were >0.01 ppm in the matrices of barley (a representative of small grains). Residue characterization of barley matrices from the 120-day rotation showed that a relatively high percentage of TRR was associated with natural plant constituents (lignin and cellulose). Therefore, tolerances are not required for rotational crops.

5.1.3 Metabolism in Livestock

The nature of the residue in animals is adequately understood based on acceptable metabolism studies conducted on ruminants and poultry. The compounds identified in these studies include dicamba, 3,6-dichlorosalicylic acid (DCSA) and 2-amino-3,6-dichlorophenol.

In a ruminant metabolism study, dicamba *per se*, accounting for 63.28-92.82% of the TRR, was detected in kidney, liver, and fat. The metabolite DCSA was a major metabolite in kidney (10.55% TRR; 0.0057 ppm) and liver (11.77% TRR; 0.0017 ppm) and only a minor component in fat (1.23% TRR; 0.0001 ppm). An unknown, accounting for <10% of the TRR was detected in liver. A trace (0.006% TRR) of 5-OH dicamba (a plant dicamba metabolite) was detected in urine. Dicamba metabolism in ruminants is proposed by the registrant to proceed via formation of DCSA or 5-OH dicamba.

In a poultry metabolism study conducted at twice the maximum theoretical dietary burden dicamba *per se* accounted for 61.16% and 95.25% of the TRR in liver and eggs, respectively. The metabolite 2-amino-3,6-dichlorophenol (2A36DCP) was detected in liver (35.76% TRR;, 0.001 ppm) but not in eggs. The metabolites DCSA and 5-OH dicamba were not detected in liver or eggs but were detected in excreta and together accounted for <3% of the TRR. Dicamba metabolism in poultry is proposed by the registrant to proceed via formation of DCSA subsequently followed by formation of 2A36DCP.

HED does not anticipate the occurrence of quantifiable residues of dicamba or DCSA in poultry eggs and meat as a result of treating crops which are poultry feed items with use patterns likely to result in the highest residues. Therefore, HED concludes that tolerances are not needed in poultry eggs and meat at this time but may be required if additional uses are registered in the future.

5.1.4 Analytical Methodology

There are adequate plant enforcement methods. The Pesticide Analytical Manual (PAM) Vol. II lists Method I (AM 0268A), a GC method with electron capture detection (GC/ECD) for the enforcement of dicamba plant tolerances. The sensitivity of the method is listed at 0.05 ppm and can determine residues of dicamba, 5-hydroxy-dicamba, and DCSA. For the enforcement of animal commodity tolerances, PAM Vol. II lists Method II, a GC/ECD method which is identical to Method I. The sensitivity of the method is listed at 0.01 ppm. Based on the results of animal metabolism study, which showed that acid hydrolysis can additionally extract up to 30% of TRR in goat liver, HED is requiring the registrants to revise/improve Method II to include an acid hydrolysis step and submit additional validation data. Method II should also be re-written specifically for the analysis of the parent dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid metabolite in animal matrices.

According to FDA's PAM Volume I, Appendix II, dicamba is completely recovered using Section 402 E2 of Protocol B but is only partially recovered using Section 402 E1 of Protocol B. There are no multiresidue methods recovery data for the dicamba metabolites of concern (5-OH dicamba and DCSA), and these data are required.

5.1.5 Environmental Degradation

Aerobic soil metabolism is the main degradative process for dicamba. A single observed half-life for dicamba was six days, with formation of the intermediate non-persistent degradate DCSA. DCSA degraded at roughly the same rate as dicamba; the final metabolites were carbon dioxide and microbial biomass. Dicamba is stable to abiotic hydrolysis at all pH's and photodegrades slowly in water and on soil. Dicamba is more persistent under anaerobic soil:water systems in the laboratory, with a half-life of 141 days. The major degradate under anaerobic conditions was DCSA, which was persistent, comprising > 60% of the applied after 365 days of anaerobic incubation. No other anaerobic degradates were present at > 10% during the incubation. There are no acceptable data for the aerobic aquatic metabolism of dicamba; supplemental information indicates that dicamba degrades more rapidly in aquatic systems when sediment is present.

Dicamba is very soluble in water and very mobile, based on laboratory studies. Because dicamba is not persistent under aerobic conditions, very little dicamba could be expected to leach to

groundwater. If any dicamba did reach anaerobic ground water, it would be somewhat persistent (due to its anaerobic half-life of 141 days); any DCSA that reached ground water would be expected to persist. Results from two acceptable field dissipation studies conducted with dimethylamine salt of dicamba, indicated that dicamba dissipated with a half-life range of 4.4 to 19.8 days. The DCSA was the major degradate in both studies. Both, dicamba and its degradate (DCSA) were found in soil segments deeper than 10 cm.

5.1.6 Comparative Metabolic Profile

Metabolism in rats appears to be less extensive than that observed in the plant and livestock metabolism studies. In the rats study rapid absorption of dicamba was observed, but minimal metabolism was observed as more than 95% of the dosing material was recovered as dicamba. Dicamba metabolism in ruminants is proposed by the registrant to proceed via formation of DCSA or 5-OH dicamba. Dicamba metabolism in poultry is proposed by the registrant to proceed via formation of DCSA subsequently followed by formation of 2A36DCP. DCSA and 5-OH-dicamba were major plant metabolites, and DCSA was the only significant environmental degradate that could potentially be found in drinking water.

5.1.7 Pesticide Metabolites and Degradates of Concern

A summary of dicamba metabolites and environmental degradates to be included in the dietary risk assessment and tolerance expression may be found in Table 5.2. DCSA and 5-OH- dicamba are major metabolites, and in the case of DCSA, a major degradate that could potentially be found in drinking water. Specific toxicity data are not available for either of these compounds. Based on their structural similarity to the parent, the risk assessment team has concluded that they may have similar toxicity as the parent, and should be included in the dietary risk assessment.

Table 5.2 Summary of Dicamba Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression [1]

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop - Most grains	Dicamba and 5-OH Dicamba	Dicamba and 5-OH Dicamba
	Primary Crop - Asparagus	Dicamba and DCSA	Dicamba and DCSA
	Primary Crop - Soybean and Aspirated Grain Fractions	Dicamba, DCSA, and 5-OH Dicamba	Dicamba, DCSA, and 5-OH Dicamba
	Rotational Crop	Not Required [2]	Not Required [2]
Livestock	Ruminant	Dicamba and DCSA	Dicamba and DCSA
	Poultry	Not Required	Not Required

Table 5.2	**Summary of Dicamba Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression** [1]	
Matrix	Residues included in Risk Assessment	Residues included in Tolerance Expression
Drinking Water	Dicamba and DCSA	Not Applicable

[1] Nomenclature of metabolites/degradates: 3,6-dichloro-5-hydroxybenzoic acid = 5-OH; 3,6-dichloro-2-hydroxybenzoic acid = 3,6-dichlorosalicylic acid = DCSA;
[2] Tolerances and dietary risk assessment are not required provided the registrants specify a 120-day plant-back interval.

5.1.8 Drinking Water Residue Profile

5.1.8.1 Surface Water

PRZM-EXAMS simulations were conducted for Dicamba acid and its degradate DCSA use on sugarcane to evaluate the cumulative probability distribution for peak and annual mean Estimated Drinking Water Concentrations (EDWCs). A summary of the EDWCs may be found in Table 5.3.

Table 5.3. Estimated Drinking Water Concentrations to Be Used for Exposure to Dicamba Acid, and its Degradate Dichlorosalicylic Acid (DCSA) in Drinking Water						
Crop	Model EDWCs (µg/L)					
	Dicamba			DCSA		
	Acute	One-in-10-year annual mean	36 year overall mean	Acute	One-in-10-year annual mean	36 year overall mean
Surface Water						
FL-Sugarcane (Ground)	357	13	5.23	10.1	0.75	0.4
FL-Sugarcane (Aerial)	346	12.9	5.38	10.9	0.813	0.47
LA-Sugarcane (Ground)	233	9.74	3.13	8.79	0.66	0.32
LA-Sugarcane (Aerial)	230	9.74	3.44	9.74	0.73	0.39
Note that these estimates assume one application @ 2.8 lb ai/A (parent); and 0.446 lb ai/A (DCSA) and a crop area factor of 0.87.						

5.1.8.2 Ground Water

SCIGROW (Screening Concentration in Ground Water) provides a groundwater screening exposure value to be used in determining the potential risk to human health from drinking water contaminated with the pesticide. Since the SCIGROW concentrations are likely to be approached in only a very small percentage of drinking water sources, i.e., highly vulnerable aquifers, it is not appropriate to use SCIGROW for national or regional exposure estimates.

SCIGROW estimates likely groundwater concentrations if the pesticide is used at the maximum allowable rate in areas where groundwater is exceptionally vulnerable to contamination. In most cases, a large majority of the use area will have groundwater that is less vulnerable to contamination than the areas used to derive the SCIGROW estimate. The EDWC for dicamba is 0.016 µg/L and for DCSA is 0.008 µg/L.

Monitoring data are available in the Pesticides in Ground Water Database [Hoheisel et al. 1991] for dicamba (3,172 wells sampled) and 5-hydroxy dicamba (87 wells sampled). Out of the wells sampled, there were no reports of residues greater than the stated MCL (200 µg/L lifetime). Detections were ranging from traces to 44 ppb. The highest detection was for water samples in IN. However, the detection limits are unknown, and it is not known if wells were sampled in areas where dicamba was used. The US Geological Survey National Water Quality Assessment program (NAWQA) has analyzed for dicamba in their samples for surface and groundwater. A total of 6614 surface water samples were collected between 1993 and 2003 with 201 detections ranging from 0.009 to 1.76 ppb. The highest detection was for water samples in FL. A total of 6571 ground water samples were collected between 1993 and 2004, with 149 detections ranging from 0.008 to 2.50 ppb. The highest detection was for water samples in GA. The major degradate for dicamba, DCSA was not analyzed for by the NAWQA.

The highest value found in the Pesticides in Ground Water Database is higher than the modeled value. Therefore, a scoping assessment using the highest monitoring value was conducted.

5.1.9 Food Residue Profile

Tolerance-level residues and 100% crop treated were assumed for all crops in this assessment. If sufficient data were available to reassess tolerances, then the reassessed values were used. The established values were used for most commodities with the exception of the livestock commodities and sorghum. All processing factors were assumed to be 1, though the available processing data suggest that residue concentrations are reduced upon processing. The tolerance reassessment summary may found in Appendix C of this document.

5.1.10 International Residue Limits

No Codex MRLs have been established for dicamba; therefore, issues of compatibility between Codex MRLs and U.S. tolerances do not exist. Compatibility cannot be achieved with the Canadian negligible residue limits or with Mexican MRLs because these levels are expressed in terms of parent compound only.

5.2 Dietary Exposure and Risk

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 2.03), which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analyses were performed to support the reregistration eligibility decision - Phase I. Results of the analyses for food alone may be found in Table 5.4 and for food and drinking water from surface water sources may be found in Table 5.5. The latter table also includes a scoping assessment for chronic dietary exposures using the highest value found in the Pesticides in Ground Water database.

Table 5.4. Summary of Dietary Exposure and Risk for Dicamba - Food Only

Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.0297	3.0	0.0115	2.6
All Infants (< 1 year old)	0.0516	5.2	0.0189	4.2
Children 1-2 years old	**0.0536**	**5.4**	**0.0292**	**6.5**
Children 3-5 years old	0.0483	4.8	0.0266	5.9
Children 6-12 years old	0.0354	3.5	0.0182	4.1
Youth 13-19 years old	0.0233	2.3	0.0111	2.5
Adults 20-49 years old	0.0214	2.1	0.00946	2.1
Adults 50+ years old	0.0150	1.5	0.00721	1.6
Females 13-49 years old	0.0180	2.9	0.00843	1.9

*The population subgroup that has the most exposure is bolded.

Table 5.5. Summary of Dietary Exposure and Risk for Dicamba - Food and Water

Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary - Surface Water		Chronic Dietary - Ground Water	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.0435	4.4	0.0118	2.6	0.0124	2.7
All Infants (< 1 year old)	**0.108**	**11**	0.0199	4.4	0.0217	4.8
Children 1-2 years old	0.0756	7.6	**0.0297**	**6.6**	**0.030**	**6.8**
Children 3-5 years old	0.0675	6.8	0.0270	6.0	0.0278	6.2

Table 5.5. Summary of Dietary Exposure and Risk for Dicamba - Food and Water						
Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary - Surface Water		Chronic Dietary - Ground Water	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*	Dietary Exposure (mg/kg/day)	% cPAD*
Children 6-12 years old	0.0476	4.8	0.0185	4.1	0.019	4.2
Youth 13-19 years old	0.0318	3.2	0.0113	2.5	0.0117	2.6
Adults 20-49 years old	0.0341	3.4	0.00973	2.2	0.0102	2.3
Adults 50+ years old	0.0267	2.7	0.00750	1.7	0.00804	1.8
Females 13-49 years old	0.0312	3.1	0.00870	1.9	0.00922	2.0

*The population subgroup that has the most exposure is bolded.

Estimated exposure to dicamba and its residues of concern for all population sub-groups are all well below the level of concern. The most highly exposed subgroup for both acute and chronic exposure is children, aged 1-2. Acute exposures are at 5.4 and 7.6% of the acute Population Adjusted Dose (aPAD) for food and food plus water, respectively. Chronic exposures are at 6.5, 6.6 and 6.8% of the chronic Population Adjusted Dose (cPAD) for food, food plus drinking water (from surface water sources), and food plus drinking water (from ground water sources) respectively. When considering acute exposure in food and water combined, the most highly exposed subgroup is infants with 11% of the aPAD consumed.

Actual exposure is likely to be considerably lower. These assessments assume all commodities have tolerance level residues, but residues in most field trials are lower. The assessments also assume all crops are treated, but a screening level usage analysis (M. Kaul, 9/20/04) indicate that the percent crop treated for most commodities is less than 20 %. Only drinking water from surface water sources were considered, but the model estimates for ground water are much lower than surface water estimates.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

According to the EPA Pesticide Sales and Usage Report for 2000/2001, dicamba is ranked number seven among the ten most commonly used conventional pesticide active ingredients in the home and garden market sector.

The residential products are typically formulated as dry weed and feed products or as liquids in concentrates or ready to use sprays. Many of these formulations include other herbicides such as 2,4-D and MCPP-p. Both spot and broadcast treatments are included on the labels. Exposures are expected to be short term in duration for broadcast treatments because the label allows only two broadcast treatments per year. Exposures are also expected to be short term in duration for

spot treatments because the labels recommend repeat applications in two to three weeks for hard to kill weeds.

6.1 Residential Handler Exposure and Risk Estimates

6.1.1 Residential Handler Exposure Assessment

Scenarios

The following scenarios were assessed:

1. Hand Application of Granules
2. Belly Grinder Application
3. Load/Apply Granules with a Broadcast Spreader
4. Mix/Load/Apply with a Hose-end Sprayer (Mix your own)
5. Mix/Load/Apply with a Hose-end Sprayer (Ready to Use)
6. Mix/Load/Apply with Hand Held Pump Sprayer
7. Mix/Load/Apply with Ready to Use Sprayer

Data Sources

The handler exposure data were taken from the Pesticide Handler Exposure Database (PHED) and the Outdoor Residential Exposure Task Force (ORETF). Exposure data for scenarios #1 and #2 were taken from PHED. Exposure data for scenarios #3, #4 and #5 were taken from the residential portion of the ORETF Handler Study. Exposure data for scenarios #6 and #7 were taken from MRID 444598-01, which has recently been purchased by the ORETF. This study involved low pressure handwand and RTU trigger sprayer application of carbaryl to home vegetable plants.

Assumptions Regarding Residential Applicators

- Clothing would consist of a short-sleeved shirt, short pants and no gloves.
- Broadcast spreaders and hose end sprayers would be used for broadcast treatments and the other application methods would be used for spot treatments only.
- An area of 0.023 acre (1000 square feet) would be treated per application during spot treatments and an area of 0.5 acre would be treated during broadcast applications.
- The application rate is 1.0 lb ae/acre as listed in the Dicamba Use Closure Memo.

6.1.2 Residential Handler Risk Estimates

A summary of the margin of exposure (MOE) estimates is included in Table 6.1. All of the MOEs exceed the target MOE of 100 and the risks are not of concern. The residential handler risks were calculated using standard assumptions, the highest quality unit exposure data available, and the maximum label application rates.

Table 6.1 Dicamba Short Term MOEs for Homeowner Applications to Lawns (Application Rate = 1.0 lb ai/acre)			
Scenario	**Treated Area (acres/day)**	**Combined Dose (mg/kg/day)**	**Combined MOE[A]**
1. Hand Application of Granules	0.023	0.0058	7800
2. Belly Grinder Application	0.023	0.0054	8300
3. Load/Apply Granules with a Broadcast Spreader	0.5	0.00073	62000
4. Mix/Load/Apply with a Hose-end Sprayer (Mix your own)	0.5	0.012	3800
5. Mix/Load/Apply with a Hose-end Sprayer (Ready to Use)	0.5	0.0029	16000
6. Mix/Load/Apply with Hand Held Pump Sprayer	0.023	0.0019	24000
7. Mix/Load/Apply with Ready to Use Sprayer	0.023	0.0027	17000
A. The target MOE is 100.			

6.2. Residential Postapplication Exposure and Risk Estimates

6.2.1 Residential Postapplication Exposure Assessment

Scenarios

The following exposure scenarios are assessed for residential post application risks

- Acute and Short Term Exposures of Toddlers Playing on Treated Turf
- Acute and Short Term Exposures of Adults Performing Yardwork on Treated Turf
- Acute and Short Term Exposures of Adults Playing Golf on Treated Turf
- Acute Exposures of Toddlers from Incidental Oral Ingestion of Granules

Data Sources

There are three turf transferable residue studies (MRID 446557-02, 450331-01 and 446557-03 that were submitted by the Broadleaf Turf Herbicide TFR Task Force. The field portion of the studies were conducted by Grayson Research LLC of Creedmoor, North Carolina, AGSTAT of Verona, Wisconsin, and Research for Hire of Porterville, California. The laboratory analysis for all three studies was conducted by Covance Laboratories of Madison, Wisconsin. These studies measured the dissipation of several phenoxy herbicides, including Dicamba, using the ORETF roller technique (which is also called the modified California Roller).

There was an additional study (MRID 449590-01) that was submitted by Novartis Crop Protection. The field portion of this study was conducted by Research Options, Inc of Winter Garden, Florida, ABC Laboratories California of Madera, California and Crop Management Strategies of Germansville, PA. The laboratory analysis for all three sites was conducted by ABC Laboratories of Columbia, Missouri. This study also used the ORETF roller technique.

All of the studies were reviewed by HED and were found to meet all of the series 875 guidelines for postapplication exposure monitoring.

Application of the TTR Data

A summary of the data used for exposure assessment is included in Table 9.2

Table 6.2 - Summary of TTR Data Used for Post Application Exposure Assessment		
MRID	**449590-01**	**450331-01**
Location	Florida	California
Precipitation	No Rain	No Rain
Application Rate (lb ae/acre)	1.0	0.21
Maximum TTR (ug/cm^2)	0.29	0.033
Maximum TTR (percent of application rate)	2.6 - Note 1	1.3
Day 0 Average TTR (ug/cm^2)	0.10	0.033
Day 0 Average TTR (percent of application rate)	0.90	1.3 - Note 2
Semi-log Slope Factor	N/A	-0.38 - Note 2
7 day Average TTR (ug/cm^2)	N/A	0.013
7 day Average TTR (percent of application rate)	N/A	0.55 - Note 2
Note 1 - This value was used to derive the TTR for 1day acute exposures. Note 2 - These values were used to derived the TTR for seven day average short term exposures.		

General Assumptions

The following general assumptions are taken from the Standard Operating Procedure (SOPs) of December 18, 1997 and ExpoSAC Policy #12 "Recommended Revisions to the Standard Operating Procedures for Residential Exposure Assessments of February 22, 2001.

- The TTR values were used for calculating dermal exposures on turf because they were greater than 1.0% of the application rate. These values were adjusted for application rates as needed
- An assumed initial TTR value of 5.0% of the application rate is used for assessing hand to mouth exposures.
- An assumed initial TTR value of 20% of the application is used for assessing object to mouth exposures.
- Soil residues are contained in the top centimeter and soil density is 0.67 mL/gram.
- Three year old toddlers are expected to weigh 15 kg.
- Hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm^2 representing the palmar surfaces of three fingers.
- Saliva extraction efficiency is 50 percent meaning that every time the hand goes in the mouth approximately ½ of the residues on the hand are removed.

- Adults are assessed using a transfer coefficient of 14,500 cm^2/hour.
- Toddlers are assessed using a transfer coefficient of 5200 cm^2/hour.
- Golfers are assessed using a transfer coefficient of 500 cm^2/hour.
- An exposure duration of 2 hours per day is assumed for toddlers playing on turf or adults performing heavy yardwork.
- An exposure duration of 4 hours is assumed for playing golf.
- The assumed ingestion rate is 0.3 gram/day. This is based on the assumption that if 150 lbs of product were applied to a ½ acre lawn, the amount of product per square foot would be 3 g/ft^2 and a child would consume one-tenth of the product available in a square foot.
- The percent ai in granular formulations used in residential settings was assumed to be in the range of 0.1 to 1.0 percent based upon the product labels listed in OPPIN.

Assumptions Specific to Dicamba

The following assumptions that are specific to Dicamba are used for assessing residential post application exposures.

- The application rate of 1.0 lbs ae/acre as stated in the Use Closure Memo was used.

Calculation Methods

The above factors were used in the standard SOP formulas to calculate the exposures. MOEs were calculated for acute dermal and incidental oral exposures using the maximum TTR value along with the acute dietary LOAEL of 300 mg/kg/day for children and NOAEL of 62.5 mg/kg/day for females, aged 13-49. MOEs for short term exposures were calculated using the seven day average TTR value, because the short term dermal NOAEL of 45 mg/kg/day was based upon decreased pup body weight gain which did not occur until after several days of exposure.

6.2.2 Residential Postapplication Risk Estimates

The MOEs for acute exposures are summarized in Table 6.3. All of the acute MOEs for both adult and toddler exposures exceed the respective target MOEs of 100 and 300, so the risks for adults and toddler exposures are not of concern.

Table 6.3 - Acute Dicamba MOEs for Turf Exposures (Application Rate = 1.0 lb ae/acre)							
Scenario	**TTR (ug/cm^2)**	**TC (cm^2/hr)**	**Dermal MOE**	**Hand-to Mouth MOE**	**Object to Mouth MOE**	**Soil Ingestion MOE**	**Total MOE[B]**
Toddlers (BW = 15 kg)							
Playing	0.29[A]	5,200	9,900	20,000	80,000	5,900,000	6,100
Adults (BW = 70 kg)							
Yardwork Golfing	0.29[A]	14,500 500	17,000 240,000	N/A			

A. This value was derived from the maximum TTR of 2.6 percent from MRID 449590-01.
B. Total MOE = 1/((1/Dermal MOE) + (1/Hand-to-Mouth MOE)+ (1/Object-to-Mouth MOE)+(1/Soil Ingestion MOE)).

The target MOE is 300 for adult and toddler exposures.

The MOEs for short term exposures are summarized in Table 6.4. All of the short term MOEs for both adult and toddler exposures exceed the target MOE of 100.

Table 6.4. Short Term Dicamba MOEs for Turf Exposures (Application Rate = 1.0 lb ae/acre)							
Scenario	**TTR (ug/cm^2)**	**TC (cm^2/hr)**	**Dermal MOE**	**Hand-to Mouth MOE**	**Object to Mouth MOE**	**Soil Ingestion MOE**	**Total MOE[B]**
Toddler Exposures (BW = 15 kg)							
Playing	0.060[A]	5200	7,200	7,200	29,000	2,100,000	3,200
Adult Exposures (BW = 70 kg)							
Yardwork	0.060[A]	14500	12,000	N/A			
Golfing	0.060[A]	500	170,000				

A. Seven day average TTR derived from the California TTR Study MRID 450331-01.
B. Total MOE = 1/((1/Dermal MOE) + (1/Hand-to-Mouth MOE)+ (1/Object-to-Mouth MOE)+(1/Soil Ingestion MOE))

The target MOE for adult and toddler exposures is 100.

The acute margins of exposures from toddlers ingesting granules are summarized in Table 6.5. All of the MOEs exceed 300, and are not of concern.

Table 6.5 Granule Ingestion Risks for Dicamba

Percent ai	Potential Dose Rate[1] (mg/day)	Absorbed Dose[2] (mg/kg/day)	Acute MOE[3]
0.1	0.3	0.02	15000
0.5	1.5	0.1	3000
1.0	3.0	0.2	1500

1. Potential Dose Rate (PDR) = 0.3 gram/day * Percent ai* 1000 mg/gram
2. Absorbed Dose = PDR/BW
3. MOE = NOAEL/Dose where the NOAEL = 300 mg/kg/day

The calculation of acute MOEs using a maximum TTR value for toddler turf post application exposure represents a policy change, because the maximum TTR values were previously only used to calculate short term MOEs. The dicamba risk assessment team decided that the previous approach would greatly overestimate the short term risks, because the short term incidental oral and dermal endpoints were based upon effects that would only occur after several days of exposure. The team also decided that the single day exposures as represented by the maximum TTR values would be more appropriately assessed using the acute dietary endpoints. The short term exposures were assessed using the seven day average TTR values because the endpoints occurred after several days of exposure and because the TTR data were collected during a seven day time period.

The actual use rates of dicamba are typically less than the maximum label rates because dicamba is usually mixed with other herbicides such as 2,4-D and MCPP-p.

6.3 Other (Spray Drift, etc.)

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for the dicamba. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. On a chemical by chemical basis, the Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift with specific products with significant risks associated with drift.

7.0 Aggregate Risk Assessments and Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure.

7.1 Acute Aggregate Risk

Acute, or less than one day, exposures may result from consuming treated food, drinking water, or residential exposures such as yard work for adults, playing golf on treated turf, or playing in treated turf for children. Typically HED does not aggregate acute food exposures with acute residential exposures. The acute food exposure estimates consider higher food consumption with maximum residue values and the estimated drinking water estimates are high-end values as well. It is very unlikely that high end food and water exposures will occur on the same day as the maximum residential exposures.

The aggregate food and water assessment results are presented in Table 7.1. The most highly exposed subgroup is infants (<1 year old) at 11% of the aPAD, which is well below the level of concern. As stated previously, actual exposures are likely to be much lower because the food assessment assumes 100% crop treated and tolerance level residues.

Table 7.1. Aggregate Acute Assessment for Dicamba - Food and Water

Population Subgroup*	Acute Dietary (95th Percentile)	
	Dietary Exposure (mg/kg/day)	% aPAD
General U.S. Population	0.0435	4.4
All Infants (< 1 year old)	**0.108**	**11**
Children 1-2 years old	0.0756	7.6
Children 3-5 years old	0.0675	6.8
Children 6-12 years old	0.0476	4.8
Youth 13-19 years old	0.0318	3.2
Adults 20-49 years old	0.0341	3.4
Adults 50+ years old	0.0267	2.7
Females 13-49 years old	0.0312	5.0
Drinking water exposures are from surface water sources.		

7.2 Short-Term Aggregate Risk

The short term aggregate assessment considered exposures from food, water, residential handles, and residential post-application activities. Average food and water exposure estimates were used in the assessment. The residential handler scenario that resulted in the highest exposures, mix/load/apply with a (mix your own) hose-end sprayer, was used in the handler assessment. The exposures from the yardwork post-application scenario was used for the adult assessment, and the exposures from the toddler playing in turf scenario was used in the child assessment. The other scenario considered was the same adult applying dicamba with the hose-end sprayer and then doing yardwork in the treated area.

The results of all of the short-term aggregate assessments are presented in Table 7.2. HED is generally not concerned if the margins of exposure (MOEs) exceed the target, which for this assessment is 100. The MOEs for all scenarios are greater than 100 so are not of concern. As stated in the previous section, these are likely to be overestimates and the actual exposures are probably much lower.

Table 7.2. Short-Term Aggregate Risk Calculations For Dicamba

Population	Food + Water Exposure mg/kg/day	Incidental Oral Exposure, mg/day	Dermal Dose, mg/kg/day	Combined Exposure, mg/kg/day	MOE Food + Water+ Incidental Oral + Dermal
Adult Male - Handler	0.012822	0	0.0102	0.023	1950
Adult Male - Post - App	0.012822	0	0.0037	0.01652	2720
Child - Post - App	0.029662	0.0078	0.0062	0.04366	1030

Note: HED is generally not concerned if the MOE exceeds the target of 100.
The adult handler assessment is from the scenario that had the highest exposure, Mix/Load/Apply with a Hose-end Sprayer (Mix your own). The adult post-application assessment is from the yard work scenario. The exposures for the child post-application scenario are from a toddler playing on treated turf. Average food and water exposures were used in this assessment. Adult Male food consumption was used for the food and water values because they have greater exposure.

7.3 Intermediate-Term Aggregate Risk

There are no residential scenarios that would result in intermediate-term (1 month to 6 month) residential exposures. Additionally, the same toxicity study was used as the endpoint for all short-, intermediate-, and long-term assessments, so the short-term assessment is protective of all of these exposures. An intermediate-term assessment is not required.

7.4 Long-Term Aggregate Risk

There are no residential scenarios that would result in long term (greater than six month)

exposures, so only food and water need be aggregated for this assessment. Results of the chronic assessment are presented in Table 7.3.

The most highly exposed subgroup is children, aged 1-2 years old, at 6.6% of the cPAD. Again, this is an exaggerated assessment as it assumes 100 percent crop treated and tolerance-level residues. Actual exposure is likely to be much lower.

Table 7.3. Summary of Dietary Exposure and Risk for Dicamba - Food and Water

Population Subgroup*	Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.0118	2.6
All Infants (< 1 year old)	0.0199	4.4
Children 1-2 years old	**0.0297**	**6.6**
Children 3-5 years old	0.0270	6.0
Children 6-12 years old	0.0185	4.1
Youth 13-19 years old	0.0113	2.5
Adults 20-49 years old	0.00973	2.2
Adults 50+ years old	0.00750	1.7
Females 13-49 years old	0.00870	1.9

7.5 Cancer Risk

In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), dicamba is classified as "Not Likely to be Carcinogenic to Humans". This was based on negative cancer studies in rats and mice which were tested at adequate dose levels to assess the carcinogenicity of dicamba Therefore, this risk assessment is not required.

8.0 Cumulative Risk Characterization/Assessment

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to dicamba and any other substances, and dicamba does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that dicamba has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on

EPA's website at http://www.epa.gov/pesticides/cumulative/.

9.0 Occupational Exposure/Risk Pathway

9.1 Short/Intermediate Handler Risk

9.1.1 Exposure

9.1.1.1 Exposure Scenarios

Based upon the application methods for occupational uses of dicamba, the following exposure scenarios were assessed.

Mix/Load Wettable Powder
Mix/Load Water Dispersible Granules
Mix/Load Liquid Formulations
Load Granules
Aerial Application
Groundboom Application
Turfgun Application
Backpack application
Right of Way Application
Broadcast Spreader Application
Mix/Load/Apply Liquids with a Backpack Sprayer
Mix/Load/Apply Wettable Powder with a Turfgun
Mix/Load/Apply Wettable Powder with a Water Dispersible Granules
Mix/Load/Apply Liquids with a Turfgun
Load/Apply Granules with a Push Cyclone
Flag Aerial Application

9.1.1.2 Occupational Handler Exposure Assumptions and Data Sources

Exposure Assumptions

The following assumptions and factors were used in order to complete the exposure and risk assessments for occupational handlers/applicators:

- The average work day was 8 hours.
- The daily acreages treated were taken from EPA Science Advisory Council for Exposure Standard Operating Procedure #9 "Standard Values for Daily Acres Treated in Agriculture," Revised July 5, 2000. These values are listed in Table 6.
- The application rates are the maximum rates as listed in the Dicamba Use Closure Memo.
- A body weight of 70 kg was assumed because the endpoint is not gender specific.
- The inhalation absorption rate is 100%.
- Baseline PPE includes long sleeve shirts, long pants and no gloves or respirator.
- Single Layer PPE includes baseline PPE with chemical resistant gloves.
- Double Layer PPE includes coveralls over single layer PPE.
- PF5 indicates a filtering facepiece respirator (i.e. a dustmask) with a protection factor of 5 when properly fitted.

- PF10 indicates a half mask elastomeric facepiece respirator with a protection factor of 10 when properly fitted and used with appropriate cartridges.
- Only closed cockpit airplanes are used for aerial application.
- Airplane pilots do not wear chemical resistant gloves.

Handler Exposure Data Sources

The handler exposure data were taken from the Pesticide Handler Exposure Database (PHED), the Outdoor Residential Exposure Task Force (ORETF) and the California Department of Pesticide Regulation (CA DPR). The PHED data were used primarily for the large scale agricultural and forestry scenarios and the ORETF data were used for lawn care scenarios. The CA DPR data were used for the backpack applicator forest site preparation scenario where multiple applicators are supplied by a nurse tank.

9.1.2 Occupational Handler Risk Estimates and Characterization

A summary of the risk estimates for occupational handlers is presented in Table 9.1. The margins of exposure for some of the baseline exposure scenarios are below the target of 100. However, if a single layer of protection or engineering controls are added to these scenarios, then all of the occupational exposure estimates have margins of exposure exceeding 100, so none of are of risk concern.

The actual use rates of dicamba are typically less than the maximum label rates because dicamba is usually mixed with other herbicides such as 2,4-D to increase the spectrum of weeds controlled.

Only a few dicamba products are formulated as wettable powders and most of these products are packaged in water soluble bags that are used on turf.

Many of the labels require waterproof gloves instead of chemical resistant gloves. It is not known if these gloves provide adequate protection.

Table 9.1 Dicamba Handler Combined MOEs

Exposure Scenario	Crop or Site	Application Rate (lb ae/acre)	Acres/ Day	Margins of Exposure		
				Base-line	Single Layer	Engineering Control
Mixer/Loader (M/L)						
M/L WP for Groundboom	Golf Courses	1	40	130	>1000	>1000
M/L WP for Turfgun Application	turf	1	5	>1000	>1000	>1000
M/L WDG for Aerial	Fallow Land	2	1200	120	120	NA
M/L WDG for Aerial	Corn	0.5	1200	490	490	NA
M/L WDG for Groundboom	Fallow Land	2	200	740	740	NA
M/L WDG for Groundboom	Corn	0.5	200	>1000	>1000	NA
M/L WDG for Groundboom	Golf Courses	1	40	>1000	>1000	NA
M/L WDG for Turf Gun	Turf	1	100	>1000	>1000	NA

Table 9.1 Dicamba Handler Combined MOEs

Exposure Scenario	Crop or Site	Application Rate (lb ae/acre)	Acres/ Day	Margins of Exposure		
				Base-line	Single Layer	Engineering Control
M/L Liquids for Aerial	Sugar Cane	2.8	1200	**2**	200	680
M/L Liquids for Aerial	Soybeans, RPF	2	1200	**3**	280	960
M/L Liquids for Aerial	Small Grains, Corn	0.5	1200	**12**	>1000	>1000
M/L Liquids for Groundboom	Sugar Cane	2.8	200	**13**	>1000	>1000
M/L Liquids for Groundboom	Soybean, RPF	2	200	**18**	>1000	>1000
M/L Liquids for Groundboom	Small Grains, Corn	0.5	200	**72**	>1000	>1000
M/L Liquids for Groundboom	Sod Farms	1	80	**90**	>1000	>1000
M/L Liquids for Groundboom	Golf Courses	1	40	180	>1000	>1000
M/L Liquids for ROW Sprayer	Right of Way Areas	2	50	**72**	>1000	>1000
M/L Liquids for Turf Gun	Turf	1	100	**72**	>1000	>1000
M/L Liquids for Backpack Application	Forest Site Prep	2	40	**90**	>1000	>1000
Load Granulars for Broadcast Spreader	Golf Courses	1.5	40	>1000	>1000	>1000
Applicator (APP)						
Aerial Application	All crops above	0.5 to 2.8	1200	ND	ND	>1000
Groundboom Application	All crops above	0.5 to 2.8	40 to 200	>1000	>1000	>1000
ROW Application	ROW	2	50	160	500	ND
Back Pack Application	Forest Site Prep	1.0	4	ND	410	ND
Turfgun Application	Turf	1.5	5	ND	>1000	ND
Broadcast Spreader Application	Golf Courses	1.5	40	>1100	>1000	>1000
Mixer/Loader/Applicator (M/L/A)						
M/L/A Wettable Powder with Turfgun	turf	1	5	ND	>1000	>1000
M/L/A WDG with Turfgun	turf	1	5	ND	>1000	ND
M/L/A Liquid Flowables with Turfgun	turf	1	5	ND	>1000	ND
M/L/A Liquids with Backpack Sprayer	ROW, RPF	2	4	ND	970	ND
Load/Apply Granules with a Push Cyclone	turf	1	5	ND	>1000	ND
Flagger						
Flag Aerial Application	All crops above	0.5 to 2.8	1200	>470	>440	>1000

Notes:
Risk estimates are the combined dermal and inhalation exposures.

RPF = Rangeland, Pastures and Fallow Land
ROW = Rights of Way
ND = No Data Available

MOEs that are less than 100 indicate risks of concern and are highlighted in bold font.

9.2 Short/Intermediate/Long-Term Postapplication Risk

Post application Dicamba exposures can occur in the agricultural environment when workers enter fields recently treated with Dicamba to conduct tasks such as scouting and irrigation.

9.2.1 Occupational Post Application Exposure

9.2.1.1 Occupational Post Application Exposure Scenarios

Broadcast applications can be made to grass crops, such as cereal grains, which are tolerant of

dicamba. Because dicamba is typically applied once per season and the relevant agricultural scenarios occur for only a few weeks per year, it is anticipated that dicamba exposures would be primarily short term and, more rarely, intermediate term.

Potential inhalation exposures are not anticipated for the post-application worker scenarios because of the low vapor pressure of dicamba (3.4×10^{-5} mm at 25 C), and the Agency currently has no policy/method for evaluating non-dietary ingestion by workers due to poor hygiene practices or smoking. As a result, only dermal exposures were evaluated in the post-application worker assessment.

9.2.1.2 - Exposure Data Sources and Assumptions

There are three turf transferable residue (TTR) studies that were submitted by the Broadleaf Turf Herbicide TFR Task Force. A summary of the turf transfer coefficients along with characterization of the post-application scenarios as low, medium, or high exposures may be found in Table 9.2

The following assumptions were made regarding occupational post application:

- Risks were assessed using the maximum rates from the Dicamba Use Closure Memo.
- The transfer coefficients are from an interim transfer coefficient policy developed by HED's Science Advisory Council for Exposure using proprietary data from the Agricultural Re-entry Task Force (ARTF) database (US EPA, August 7, 2001). This policy will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.
- The transfer coefficients for turf harvesting and maintenance are based upon recently conducted ARTF studies that are being reviewed by HED.
- The initial percent of application rate as Dislodgeable Foliar Residue (DFR) was assumed to be 20% for all crops except turf. These are the standard values used in the absence of chemical specific data.
- The Maximum TTR value (2.6 percent of the application rate) from the DMA Treatment at the Florida site in the Vanquish Study was used to assess risks of working on turf.

Table 9.2 Post Application Exposure Scenarios and Transfer Coefficients for Dicamba

Crop	Label Directions Post Application Exposure Scenarios	Transfer Coefficient (cm^2/hr)
Asparagus	Apply immediately after cutting. If spray contacts emerged spears, crooking may result. Pre Harvest Interval (PHI) = 24 hours	None[1,2]
Small Grains Barley, Oats, proso millet, triticale, wheat	Apply to fall seeded barley prior to the jointing stage. Apply to spring seed barley before it exceeds the 4 leaf stage. Apply to fall seeded oats prior to the jointing stage. Apply to spring seeded oats before the 5 leaf stage is exceeded. Apply to proso millet at the 2 to 5 leaf stage. Apply to fall seeded triticale or wheat prior to the jointing stage. Apply to spring seeded triticale or wheat before the 6 leaf stage. Low Exposure Scenarios - Irrigation, scouting, immature plants Medium Exposure Scenarios - Same as above on mature plants	 100 1500
Corn	Early Post Emergence - Apply from corn emergence through 5 leaf stage or 8 inches tall, whichever comes first. Late Post Emergence - Apply from 8 to 36 inch corn or to 15 days before tassel emergence, whichever comes first. Low Exposure Scenarios - Scouting, weeding immature plants Medium Exposure Scenarios - Scouting, weeding more mature plants High Exposure Scenarios - Scouting, weeding, irrigation mature plants Very High Exposure Scenarios - Detasseling	 100 400 NA NA
Cotton	N/A - Applied as a preplant treatment.	NA
Pasture, Rangeland, Grassland	PHI = 7 days	None[1]
Sorghum	Post Emergence - Apply when sorghum is in the 3 to 5 leaf stage, but before it is 15" tall. If sorghum is taller than 8" use drop nozzles and keep spray off the foliage Pre-harvest application (TX and OK only) - apply anytime after soft dough stage (PHI = 30 days) Low Exposure Scenarios - Scouting immature plants High Exposure Scenarios - Irrigation and scouting mature plants	 100 1000
Soybeans	Apply after pods have reached mature brown color and at least 75% leaf drop has occurred (PHI = 14 days)	None[1]
Sugarcane	Apply before canes appear for control of emerged weeds. Apply after canes emerge and through canopy closure. When possible direct sprays beneath the canopy to minimize the likelihood of crop damage. Medium Exposure Scenarios - scouting immature plants High Exposure Scenarios - scouting mature plants	 1000 2000
Turf, Sod Farm and Golf Course	Treat when weeds are young and actively growing. Do not apply more than 1.0 lb per season. Low Exposure Scenarios - Mowing High Exposure Scenarios - Transplanting, hand weeding	 3400 6800

1. Post application exposures are expected to be minimal due to application timing or method.
2. Asparagus plants do not have foliage (i.e. ferns) when the spears are harvested.

9.2.2 Occupational Post Application Risk Estimates

A summary of the worker risks for short/intermediate term post application exposures is given in Table 9.3. All of the short/intermediate term MOEs are above 100 on Day 0 which indicates that

the risks are not of concern. The Worker Protection Standard (WPS) Restricted Entry Interval (REI) for dicamba is 24 hours for the amine and sodium salt forms.

Table 9.3 - Dicamba Postapplication Worker Risks

Crop	Transfer Coefficient Group	Application Rate (lb ae/acre)	Short/Intermediate Term MOE on Day 0		
			Low Exposure Scenarios*	Medium Exposure Scenarios*	High Exposure Scenarios*
Small Grains (i.e. wheat)	Field/row crop, low/medium	0.50	23000	1600	NA
Corn (Early Post Emergence)	Field/row crop, low/medium	0.50	23000	N/A	NA
Corn (Late Post Emergence)	Field/row crop, low/medium	0.25	N/A	12000	N/A
Sorghum	Field/row crop, low/medium	0.25	47000	12000	4700
Sugarcane	Sugarcane	2.8	N/A	420	210
Turf	Turf	1.0	2600	N/A	1300

10.0 Data Needs and Label Requirements

10.1 Toxicology

No studies are required.

10.2 Residue Chemistry

- Additional method validation data using Method AM-0691B-0297-4; recovery data are needed for barley grain and straw at fortification levels of 6 and 15 ppm, respectively, and for wheat straw at 30 ppm. Additional method validation data using Method AM-0941-1094-0 are also needed for soybean seeds at a spike level of 10 ppm.

- Revise/improve Method II of PAM Vol. II to include an acid hydrolysis step and submit additional validation data. Method II should also be re-written specifically for the analysis of the parent dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid metabolite in animal matrices.

- Multiresidue methods recovery data for the dicamba metabolites of concern (5-OH dicamba and DCSA).

- Storage stability data for sugarcane molasses and animal commodities.

- Residue data and tolerances for soybean forage and hay if no feeding restrictions appear on the label.

- Magnitude of the residue data for sugarcane. In lieu of submitting additional data the registrants have the option of relying on the available/submitted data provided they revise their product labels for consistency with the reviewed data.

10.3 Occupational and Residential Exposure

No Data Required

References

Abdel-Saheb, I., **Drinking water assessment for Dicamba on sugarcane**; PC Code 029801; DP Barcode: 317705; May 31, 2005.

Dole, T. **Dicamba:** Occupational and Residential Exposure and Risk Assessment for the Reregistration Eligibility Decision (RED) Document ; PC Code 029801, DP Barcode D317701; August 2005.

Hartge P, Colt JS, Severson RK, et al. 2005. Residential herbicide use and risk of non-Hodgkin's lymphoma. Cancer Epidemiology, Biomarkers and Prevention 14:934-7.

Hawkins, M.; Review of Dicamba Incident Reports; Chemical #029801; DP Barcode D316974; July 28, 2005.

Kaul, M.; Screening Level Usage Analysis for Dicamba, 9/20/04.

Kidwell, J.; DICAMBA: Report of the Dose Adequacy Review Team. PC Code: 029801. DP Barcode: DP 317700; 8/16/2005.

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Olinger, C., **Dicamba:** Acute and Chronic Dietary Exposure Assessments for the Reregistration Eligibility - Phase 1; PC Code: 029801; DP Barcode: D317702; August 2005.

Olinger, C., **Dicamba:** Residue Chemistry Considerations for the Reregistration Eligibility Decision (RED) Document; PC Code: 029801; DP Barcode: D317703; August 2005.

Appendix A: Toxicology Assessment

Table A3. Data requirements (CFR 158.340) for Dicamba

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	Oral Subchronic (rodent)	yes	yes[1]
870.3150	Oral Subchronic (nonrodent)	yes	yes[1]
870.3200	21-Day Dermal	yes	yes
870.3250	90-Day Dermal	no	NA
870.3465	90-Day Inhalation	no	NA
870.3700a	Developmental Toxicity (rodent)	yes	yes
870.3700b	Developmental Toxicity (nonrodent)	yes	yes
870.3800	Reproduction	yes	yes
870.4100a	Chronic Toxicity (rodent)	yes	yes
870.4100b	Chronic Toxicity (nonrodent)	yes	yes
870.4200a	Oncogenicity (rat)	yes	yes
870.4200b	Oncogenicity (mouse)	yes	yes
870.4300	Chronic/Oncogenicity	yes	yes
870.5100	Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5375	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5xxx	Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a	Acute Delayed Neurotox. (hen)	no	no
870.6100b	90-Day Neurotoxicity (hen)	no	no
870.6200a	Acute Neurotox. Screening Battery (rat)	yes	yes
870.6200b	90 Day Neuro. Screening Battery (rat)	yes	yes
870.6300	Develop. Neuro	yes	yes
870.7485	General Metabolism	yes	yes
870.7600	Dermal Penetration	yes	yes
Special Studies for Ocular Effects			
	Acute Oral (rat)	no	no
	Subchronic Oral (rat)	no	no
	Six-month Oral (dog)	no	no

1. Requirements are satisfied by chronic oral toxicity studies.

Summaries of Carcinogenicity and Mutagenicity Studies

Carcinogenicity Study in Rats

Executive Summary: In a combined chronic toxicity/carcinogenicity study (MRID 00146150), groups of 60 male and 60 female CD rats were fed diets containing dicamba (86.8% a.i.; Lot no. 52625110) at 0, 50, 250 ro 2500 ppm for 115 (males) or 117 (females) weeks. These doses

correspond to 0, 2, 11 or 107 mg/kg bw/day for males and 0, 3, 13 or 127 mg/kg bw/day for females. Treatment had no adverse effect on survival, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, organ weights or gross pathology. Histopathology revealed increases in malignant lymphomas in males (0/60, 0/60, 4/60 and 4/60 at 0, 50, 250 and 2500 ppm, respectively) and thyroid parafollicular cell carcinomas in males (1/60, 0/60, 2/60 and 5/60 at 0, 50, 250 and 2500 ppm, respectively). The Cochran-Armitage trend test showed a statistically significant ($p \leq 0.05$) tendency for the proportion of animals with tumors to increase steadily with increase in dose. Pairwise comparison (Fisher's Exact test) showed no statistical significance. Therefore, these tumors were not considered to be toxicologically significant.

Under the conditions of this study, dicamba was not carcinogenic in male or female rats at the doses tested. The lack of systemic toxicity indicate that the animals may have tolerated higher doses (i.e., an MTD was not achieved). However, the doses employed in this study were approved by the Agency (Memo: S. April to R. Taylor, RD, dated 09/26/86).

Discussion of Tumor Data:
The administration of dicamba to rats up to 2500 ppm (107 mg/kg/day for males, 127 mg/kg/day for females) in the diet revealed increases in malignant lymphomas in males (0/60, 0/60, 4/60 and 4/60 at 0, 50, 250 and 2500 ppm, respectively) and thyroid parafollicular cell carcinomas in males (1/60, 0/60, 2/60 and 5/60 at 0, 50, 250 and 2500 ppm, respectively). The Cochran-Armitage trend test showed a statistically significant ($p \leq 0.05$) tendency for the proportion of animals with tumors to increase steadily with increase in dose. Pairwise comparison (Fisher's Exact test) showed no statistical significance. Therefore, these tumors were not considered to be toxicologically significant.

Adequacy of the Dose Levels Tested:

The Dose Adequacy Review Team (DART) reviewed the dosages of the study and concluded that the dose levels in the chronic toxicity/carcinogenicity study in rats could have been higher based on kinetics data which indicated that saturation of excretion occurred at a dose ranging from >200 to 400 mg/kg/day. However, retesting at a dose greater than 300 mg/kg/day, for example, would not be recommended based on the saturation data, which showed evidence of saturation of excretion at >200 mg/kg/day. Retesting at a dose of 300 mg/kg/day would not be expected to alter the conclusion that there was no carcinogenic effect. Since the doses in the rat carcinogenicity study (107/127 mg/kg/day) were within a factor of around two fold of the saturation point (>200-400 mg/kg/day), the doses were considered to be adequate for assessment of carcinogenicity. Therefore, the DART concluded that a new chronic toxicity/carcinogenicity study in the rat was not required (TXR No. 0053647).

Carcinogenicity Study in Mice

Executive Summary:
In a carcinogenicity study (MRID 40872401), groups of 52 male and 52 female CD-1 mice were fed diets containing dicamba (86.8% a.i.; Lot no. 52625110) at 0, 50, 150, 1000 or 3000 ppm for 89 (males) or 104 (females) weeks. These doses correspond to 0, 5.5, 17.2, 108 or 358 mg/kg

bw/day for males and 0, 5.8, 18.8, 121 or 354 mg/kg bw/day for females. Mortality was significantly increased in males at 150 ppm and at 3000 ppm; the cause of mortality was amyloidosis. The incidence of this lesion was higher than any other single factor among males that died in all groups especially the high dose. Except for a significant decrease at 150 ppm, survival among treated females was comparable to that of the controls. Body weight gain was higher in treated males than control males while there was a 17% decrease in body weight gain in females at 3000 ppm. No treatement-related effects were seen in food consumption, hematology, organ weights or gross pathology. Histopathology revealed a statistically significant ($p < 0.05$) increase in lymphosarcomas in females at 150 ppm only (8/52, 15%) compared to controls (2/52, 4%). The increase was not considered to be treatment-related due to lack of a dose-response and the incidences were within the historical control range (6-33%). Additionally, the incidence in the concurrent control (4%) was below the historical range.

Under the conditions of this study, dicamba was not carcinogenic in male or female mice at the doses tested. The lack of systemic toxicity indicate that the animals may have tolerated higher doses (i.e. and MTD was not achieved). However, the doses employed in this study were approved by the Agency (Memo: S. April to R. Taylor, RD, dated 11/15/84).

Discussion of Tumor Data:
The administration of dicamba to mice up to 3000 ppm (358 mg/kg/day for males, 354 mg/kg/day for females) in the diet revealed a statistically significant ($p < 0.05$) increase in lymphosarcomas in females at 150 ppm only (8/52, 15%) compared to controls (2/52, 4%). The increase was not considered to be treatment-related due to lack of a dose-response and the incidences were within the historical control range (6-33%). Additionally, the incidence in the concurrent control (4%) was below the historical range.

Adequacy of the Dose Levels Tested:

The DART revisited the 1995 decision by the RfD/Peer Review Committee that the mouse carcinogenicity study was not tested at a high enough doses to evaluate carcinogenicity in the mouse. The DART concluded that 3000 ppm is an adequate dose in the mouse cancer study and decided that a new mouse carcinogenicity study was not needed (TXR No. 0053647).

Mutagenicity

The RfD/Peer Review Committee reviewed the toxicology database of dicamba and determined that mutagenicity studies satisfied the minimum mutagenicity testing as per the pre-1991 guidelines (TXR No. 0012037, 7/29/96). Results are summarized as follow: negative for Ames (Salmonella), negative for WPU (E. Coli WP2), negative for SRL (sex-linked recessive lethal in Drosophila), negative for YE3 (S. cerevisiae mitotic recombination in strain D3), negative for UDH (UDS with WI-38 human lung fibroblasts), negative for SAR (differential toxicity with S. typhimurium), negative for chromosome aberration in the CHO cells; positive for REP (differential toxicity with E. Coli polA), positive for REW (differential toxicity with B. subtilis). Other published studies included positive UDS in cultured human lymphocytes w/S9, slight increase of SCE in cultured human lymphocytes with plus -minus activity; positive in an in vivo

assay for unwinding of liver DNA in i.p. injected rats (Environ Milec Mutagen 15: 131-135, 1990); negative for Salmonella and E. Coli WP2 (Mut. Res 116: 185-216, 1983); Negative for aberrations in rat bone marrow (Mut. Res 321:219-228, 1994).

Structure Activity Relationship Analysis for Carcinogenicity

The Structure Activity Relationship (SAR) showed that the concern level for carcinogenic potential is low. According to the OncoLogic Cancer Expert System, there is a Low-Moderate concern for para-dichlorobenzene but the substituents of dicamba lower the concern to Low. A structurally similar chemical, 2,4-D, is negative for carcinogenicity with a negative Ames test but positive chromosomal aberration and CHO tests. Other structurally similar chemicals, 5-chlorosalicylic acid, dichlorobenzoic acid, and chlorobenzoic acid have negative Ames tests, but no carcinogenicity data are available.

OTHER TOXICOLOGY STUDIES

Executive summaries for studies not described in the main body of the document are provided in the following pages.

In an acute neurotoxicity study (MRID 42774104) groups of Crl:CD BR rats (10/sex/dose) received a single oral (gavage) administration of dicamba (86.9%) in corn oil at doses of 0, 300, 600, or 1200 mg/kg. Vehicle controls received corn oil only. Positive controls received acrylamide at 50 mg/kg/day by intraperitoneal injection on seven consecutive days. At 300 mg/kg, transiently impaired respiration; rigidity upon handling, prodding or dropping; freezing of movement when touched; decreased arousal and fewer rears/minute compared to controls; impairment of gait and righting reflex were observed in both sexes. In addition, males showed decreased forelimb grip strength. With the exception of the decrease in forelimb grip strength, which persisted until day seven, these effects were observed only on the day of dosing. In addition, at 600 mg/kg, both sexes showed decreases in locomotor activity and males showed significant decreases in tail flick reflex and a raised posture when placed in an open field. These effects were also observed only on the day of dosing. At the highest dose level tested (1200 mg/kg), both males and females showed an impaired startle response to an auditory stimulus. The effect was significant in males on day seven and in females on the day of dosing. In addition, males showed decreases in body weight (5 - 9%), body weight gain (24%) and food consumption (13% between days 0 and 7). The LOAEL was 300 mg/kg based on the several neurologic signs listed above; a NOAEL was not established. The submitted study is classified as **acceptable/guideline** and satisfies the Guideline requirements for an acute neurotoxicity screening battery in rats.

Subchronic Neurotoxicity Study in the Rat

In a subchronic neurotoxicity study (MRID No. 43245210), Sprague-Dawley rats (10/sex/dose) were fed diets containing dicamba (86.9%) at 0, 3000, 6000, or 12000 ppm (0, 197.1, 401.4, 767.9 mg/kg/day for males and 0, 253.4, 472.0 or 1028.9 mg/kg/day for females, respectively) for 13 weeks. Neurobehavioral evaluations, consisting of FOB, locomotor activity, and auditory startle response, were conducted at prestudy and during Weeks 4, 8 and 13. No toxicologically

significant differences were noted in either the mean body weights or food consumption of the treated animals. Neurobehavioral evaluations at the 4-, 8-, and 13-week evaluations revealed abnormal FOB observations consisting of rigid body tone, slightly impaired righting reflex and impaired gait. At Week 13 the incidences of these findings were decreased. Rigid body tone was also noted during evaluation of the righting reflex and landing foot splay. The NOAEL was 401 mg/kg/day and the LOAEL was 768 mg/kg/day based on rigid body tone, slightly impaired righting reflex and impaired gait. The study is classified as **acceptable/guideline** and satisfies the guideline requirements (870.6200b) for a subchronic neurotoxicity study in the rat.

21/28-Day Dermal Toxicity – Rat (870.3200)

In a 28-day dermal toxicity study (MRID 45814501), Dicamba (91.0% a.i., batch #B2826511) was applied to the shaved skin of 10 male and 10 female Alpk:AP ,SD rats /sex/dose at dose levels of 0, 30, 300 or 1000 mg/kg bw/day, 6 hours/day for 5 days/week during a 28-day period.

Clinical observations, body weights and food consumption were measured throughout the study. Urine samples were taken for clinical pathology during week 4 of the study. A functional observational battery of all animals consisting of: detailed clinical observations, including quantitative assessments of landing foot splay, sensory perception and muscle weakness, and assessment of motor activity was performed on day 22. At the end of the scheduled period, the animals were killed and subjected to a post mortem examination. Blood samples were taken for clinical pathology, selected organs and specified tissues were taken for subsequent histopathological examination.

There were no changes indicative of systemic toxicity in either sex. There were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Histopathological changes indicative of irritation were seen in skin from the application site in both sexes given 1000 or 300 mg/kg/day and in some males given 30 mg/kg/day. **A LOAEL for systemic toxicity was not established. The NOAEL is 1000 mg/kg/day the highest dose tested.**

This 28-day dermal toxicity study in the rat is **acceptable/ guideline**, and satisfies the guideline requirement for a 28-day dermal toxicity study (OPPTS 870.3200 ; OECD 410) in the rat.

21/28-Day Dermal Toxicity – Rabbit (870.3200)

In a 21-day dermal study (MRID 40547901), New Zealand white rabbits (5/sex/group) received 15 repeated dermal applications of Dicamba in deionized water at dose levels of 0, 40, 200, or 1000 mg/kg/day , 6 hours/day, 5 days/week over a three week period. No systemic toxicity was observed at any dose level. Dose-related dermal irritation was observed at the application sites. Desquamation was seen predominantly in the 1000 mg/kg/day group while moderate erythema, moderate edema and atonia were observed exclusively in the 1000 mg/kg/day group. A dose-related incidence of fissuring was noted in the 200 and 1000 mg/kg/day groups. The severity of acanthosis and the incidence of hyperkeratosis was increased at these sites in rabbits at 200 and 1000 mg/kg. **For systemic toxicity, the NOEL was 1000 mg/kg/day (HDT); a systemic LOEL was not be established.**

This 28-day dermal toxicity study in the rat is **acceptable/ guideline**, and satisfies the guideline requirement for a 21-day dermal toxicity study (OPPTS 870.3200 ; OECD 410) in the rabbit.

Subchronic Oral Toxicity- Rat (870.3100)
In a 13-week subchronic toxicity study (MRID 44623101), dicamba technical (89.4% a.i.) was administered to HanIbm:WIST (Wistar) rats (10 or 20 rats/sex/dose) by feeding at dose levels of 0, 500, 3000, 6000, or 12,000 ppm (equivalent to 0/0, 40.1/43.2, 238.7/266.4, 479.4/535.6, or 1000.0/1065.3 mg/kg/day [M/F]) for 13 weeks. Following 13 weeks of treatment, 10 rats/sex/dose were sacrificed. Rats (10/sex) in the control and 12,000 ppm groups were maintained for a 4-week recovery period to determine the reversibility of effects.

No treatment-related deaths were observed in any treatment group. The liver was the target organ, as evidenced by microscopic liver changes associated with clinical serum chemistry changes and increased relative (to body) liver weights (↑20-23%) in both sexes at the high dose. The livers of the 12,000 ppm females exhibited slight centrolobular hepatocyte hypertrophy (4/10) and an increased incidence of minimal to moderate hepatocellular pigmentation (5/10). Both sexes exhibited increased alkaline phosphatase (↑62-76%), serum alanine aminotransferase (↑59-66%), and serum aspartate aminotransferase (↑29%) activities compared to the controls. Females exhibited an increase in mean gamma glutamyl transferase activity (↑136%) while males showed a decrease activity (↓50%) compared to the controls.

Other effects observed in the 12,000 ppm rats were transient hypothermia (weeks 1-4), reduced activity, slower movements, decreased food consumption, and less efficient food utilization than the controls throughout the treatment period. Lower mean final body weights (↓18-20%), body weight gains (↓28-40%) and adipose tissue content were observed compared to the controls. Decreases in protein (↓10-15%) and globulin (↓16-26%) levels were observed in both sexes. In females, decreased mean hemoglobin concentration (↓4%) and red blood cell counts (↓4%), and decreased mean corpuscular hemoglobin concentration (↓3%) were observed. Significant ($p<0.05$ or $p<0.01$) increases of white blood cell count (↑13%) and lymphocyte count (↑33%) were observed in 12000 ppm females compared to the controls. Males had a lower mean platelet count (↓7%) and shorter partial thromboplastin time (↓11%) compared to the controls. Urinalysis showed that males excreted more triple phosphate crystals in the 12000 ppm group, whereas females excreted more uric acid crystals in the 12000 and 6000 ppm groups at week 12. Following a 4-week recovery period, all observed effects were recovered.

The LOAEL for this study is 12,000 ppm (1000 mg/kg/day), based on clinical signs, reduced body weight gains, hematological and clinical serum chemistry changes in both sexes, centrolobular hepatocyte hypertrophy and hepatocellular pigmentation in females, and increased relative (to body) liver weights for both sexes. The NOAEL is 6000 ppm (479 mg/kg/day).

This 13-week subchronic toxicity study is classified **acceptable/guideline (870.3100)** and satisfies the guideline requirement for a subchronic toxicity study in rodents.

Chronic Toxicity - Dog (870.4100b)

In a chronic oral toxicity study (MRID 40321102), dicamba (86.8, a.i., lot # 52625110) was administered to beagle dogs (4/sex/group) in diet at dose levels of 0, 100, 500, or 2500 ppm (0, 2, 11, or 52 mg/kg/day, respectively) for one year.

The investiagated parameters in this study, which included behavior, mortality, body weight, food consumption, hematology, serum chemistry, urinalysis as well as macroscopic and histologic examination of tissues, did not reveal any apparent adverse effect from the test compound. Therefore, the NOAEL for dicamba was 2500 ppm in the diet (about 52 mg/kg/day), the highest dosage administered in this test; the absence of any adverse effects among treated animals indicated that the MTD was not attained.

This one-year dog study is classified **Acceptable/Guideline** and satisfies the guideline requirement for a chronic toxicity study in dogs.

Metabolism - Rat (870.7485)

In a plasma kinetics study, (MRID 44609801), [phenyl-U-^{14}C]- dicamba ([^{14}C]-dicamba; 86.0% a.i. radiochemical purity), was administered as a dietary admix to 4 male and 4 female Wistar and Sprague-Dawley at 900, 1500, 3000, 4500, and 12000 ppm (Wistar rats) and 900, 1500, 3000, 6000 and 9000 ppm (Sprague-Dawley rats) for fourteen days, followed by a radioactive dose of 90, 150, 300, 450 mg/kg bw (Wistar rats) and 75, 125, 250, 500 and 800 mg/kg bw by a single gavage dose (in 10 ml/kg body weight 0.5% Tylose CB 30.000 in aqua bidest). Plasma levels were measured at various time intervals following radioactive dose.

A preliminary study in Wistar rats suggests excessive toxicity following repeated gavage doses. Therefore, the main study in both strains of rats was conducted as a dietary ad mix followed by a gavage dose of radiolabeled dicamba. In both strains of rats, the plasma levels reached a maximum level after 0.5-1 hour following the gavage dose and declined thereafter. The $AUC_{0-\infty}$ values were calculated from the plasma concentrations versus time curves at the respective dose levels indicated linear relationship with increase in dose up to a certain dose levels in both strains of rats indicating saturation of excretion. Initial plasma half-life was increased with increasing dose, but terminal half-life remains more or less constant in both strains of rats indicating saturation of excretion. Plasma half-life was increased with increasing dose giving no indication of saturation of oral absorption.

In Wistar rats, the increase in plasma AUC was linear with dose up to a level of 150 mg/kg bw in males and 300 mg/kg bw in females. Above these dose levels, plasma AUC-values increased more than dose. Sprague-Dawley rats showed similar results, with the increase in AUC being linear with dose up to a level of 125 and 250 mg/kg bw in males and females, respectively. Above these dose levels, plasma AUC-values increased more than dose. Considering that oral absorption was not saturated and that initial plasma levels went up with dose, the disproportionate increase in plasma AUC is clearly due to saturation of renal excretion of dicamba resulting in a longer plasma half-life. This is supported by half-life data in both species which showed an increase in plasma half-life with dose.

This plasma kinetics study in the rats is classified **Acceptable/Nonguideline (§85-1).**

Metabolism - Rat (870.7485)

In a plasma pharmacokinetic study (MRID 46022302), five groups of 4 male and 4 female Wistar rats received diets containing the equivalent of 50, 100, 200, 400, or 800 mg/kg dicamba/day for 90 days (Lot No. 52103810, 87.2% a.i.) . On study days 29, 63, and 91, dietary supplementation of dicamba was stopped and rats in each group received an equivalent gavage dose of ^{14}C-dicamba (Lot No. 787-0102, >99% a.i., universally labeled in the phenyl group). Blood samples were drawn 0.5, 1, 2, 4, 6, 8, 12, 24, and 48 hours after treatment and the plasma radioactivity determined.

Absorption of the radiolabeled test material was rapid, with peak plasma concentrations found within 2 hours of treatment. Absorption was not saturated, even at the highest dose, as indicated by increasing plasma concentrations with dose. However, the increase in plasma concentration was disproportionate from dose as shown by the ≥ 2-fold increase in AUC from one dose group to the next at doses >100 mg/kg. Elimination of radiolabel from the plasma was tri-phasic, with the terminal-phase consistent between doses. However, the initial elimination phase increased with dose, particularly in the 400 and 800 mg/kg dose groups and is consistent with excretion saturation. No significant treatment-related differences between the sexes or time of radiolabel administration were found.

This plasma pharmacokinetic study in the rat is classified **Acceptable/Nonguideline** and satisfies its intent.

Metabolism - Rat (870.7485)

In a pharmacokinetic study (MRID 46022303), two groups of 3 male Wistar rats were given a single 200 mg/kg gavage dose of ^{14}C-dicamba (Lot No. 787-0102, >99% a.i., universally labeled in the phenyl group). One group of rats was pretreated with a 150 mg/kg IP dose of probenecid , a known competitive inhibitor of renal anion transport, 30 minutes prior to dicamba dosing. Blood samples were drawn 0.5, 1, 2, 4, 6, 8, 12, 24, and 48 hours after gavage treatment and the plasma radioactivity determined.

The time to peak plasma concentration in rats treated with ^{14}C-dicamba occurred within 0.5 hours while peak plasma concentration was reached at 1.0 hour in the probenecid/dicamba rats. However, pretreatment with probenecid increased plasma AUC by a factor of 1.54. Although the terminal phase of elimination remained relatively the same, the initial and intermediate elimination phases were increased by a factor of two. These data suggest that both dicamba and probenecid, act as inhibitors of renal anion transport.

This pharmacokinetic study in the rat (MRID 46022303) is classified **Acceptable/Nonguideline** and satisfies its intent.

Appendix B: Use Profile

Table B.1 Dicamba Use Profile (8/2/2005)			
Use Sites	Forms[1]	Max Application Rate (Unit/Area)	Max Application Rate (year)
Non-Food/Non-Feed Uses			
Agricultural Fallow/Idleland (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Agricultural rights-of-way/fencerows/hedgerows (Non-crop)[2]	Dimethylamine Salt, Sodium Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A)
		7.7 (lbs a.e./A)	7.7 (lbs a.e./A)
Agricultural Uncultivated Areas (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Agricultural/Farm Structures/Buildings and Equipment (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Airports/Landing Fields (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Commercial/Industrial Lawns (Non-crop)	Dimethylamine Salt	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Commercial/Institutional/ Industrial Premises/Equipment (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Drainage Systems (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Fencerows/Hedgerows (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Forest Plantings (reforestation programs)(tree farms, tree plantations, etc) (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Forest Trees (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Golf Course Turf	Dimethylamine Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.e./A) year
Household Domestic Dwellings (Non-crop)	Dimethylamine Salt	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Industrial Areas (Outdoor) (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Nonagricultural Outdoor Buildings/Structures (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year

Table B.1 Dicamba Use Profile (8/2/2005)			
Use Sites	Forms[1]	Max Application Rate (Unit/Area)	Max Application Rate (year)
Nonagricultural Rights-of-way/Fencerows/ Hedgerows (Non-crop)	Dimethylamine Salt, Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Nonagricultural Uncultivated Area/Soils (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Ornamental Lawns and Turf	Dimethylamine Salt, Sodium Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.i../A) year
Ornamental Sod Farm	Dimethylamine Salt, DGA	1.0 (lbs a.e./A)	1.0 (lbs a.e./A) year
Paths/Patios (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e/A)	2.0 (lbs a.e./A) year
Paved Areas (Private Roads/Sidewalks (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e/A)	2.0 (lbs a.e./A) year
Recreation Area Lawns	Dimethylamine Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Recreational Areas	Dimethylamine Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Residential Lawns	Dimethylamine Salt	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Urban Areas (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Food/Feed Uses			
Agricultural Crops/Soils	Dimethylamine Salt, Sodium Salt	2.0 (lbs a.e/A)	2.0 (lbs a.e./A) year
Agricultural Fallow/Idleland	All	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Agricultural/Farm Premises	Dimethylamine Salt, DGA	1.0 (lbs a.e./A)	1.0 (lbs a.e./A) year
Agricultural/Farm Structures/Buildings and Equipment	Dimethylamine Salt	1.0 (lbs a.e./A)	1.0 (lbs a.e./A) year
Asparagus	Dimethylamine Salt, Sodium Salt, DGA	0.5 (lbs a.e./A)	0.5 (lbs a.e./A) year
Barley	Dimethylamine Salt, Sodium Salt, DGA, IPA	0.25 (lbs a.e./A)	0.38 (lbs a.e./A) year
Corn (field, pop, seed, silage)	Dimethylamine Salt, Sodium Salt, DGA, Potassium Salt	0.5 (lbs a.e./A)	0.75 (lbs a.e./A) year
Cotton	Dimethylamine Salt, DGA	0.25 (lbs a.e./A)	2.0 (lbs a.e./A)
Hay	Dimethylamine Salt, Sodium Salt, DGA	2.0[3] (lbs a.e./A)	2.0 (lbs a.e./A) year
Millet (Proso)	Dimethylamine Salt	0.125 (lbs a.e/A)	0.125 (lbs a.e./A) year

Table B.1 Dicamba Use Profile (8/2/2005)			
Use Sites	Forms[1]	Max Application Rate (Unit/Area)	Max Application Rate (year)
Oats	Dimethylamine Salt, Sodium Salt, DGA	0.125 (lbs a.e./A)	1.0 (lbs a.e/A) year
Pastures[4]	Dimethylamine Salt, Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
		7.7 (lbs a.e/A)	7.7 (lbs a.e/A) year
Rangeland[5]	Dimethylamine Salt, Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
		7.7 (lbs a.e./A	7.7 (lbs a.e/A) year
Rye	Dimethylamine Salt	0.5 (lbs a.e./A)	1.0 (lbs a.e./A) year
Sorghum	All	.2748 (lbs a.e./A)	0.5 (lbs a.e./A) year
Soybean	Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e/A) year
Sudangrass	Dimethylamine Salt	0.5 (lbs a.e./A) As listed for Hay.	1.0 (lbs a.e./A) year
Sugarcane	Dimethylamine Salt, Sodium Salt, DGA	2.8 (lbs a.e./A)	2.8 (lbs a.e./A) year
Wheat	Dimethylamine Salt, Sodium Salt, DGA, IPA	0.5 (lbs a.e./A)	1.0 (lbs a.e./A) year

1. There are 5 forms of dicamba used in this Master Label: Dimethylamine Salt (PC Code 29802), Sodium Salt (PC Code 29806), Diglycoamine [DGA] (PC Code 128931), Isopropylamine Salt [IPA] (PC Code 128944), and Potassium Salt (PC Code 129043)

2. Label 100-884 list 7.7 lbs a.e./A as the maximum rate for spot treatment for Agricultural right-of-way uses. The 2.0 lbs a.e./ A is what the registrant stated at the SMART Meeting as the rate they intended to support.

3. Based on label 51036-289 and 7969-131

4. Label 100-884 list 7.7 lbs a.e./A as the maximum rate for spot treatment for pasture uses. The 2.0 lbs a.e./ A is what the registrant stated at the SMART Meeting as the rate they intended to support.

5. Label 100-884 list 7.7 lbs a.e./A as the maximum rate for spot treatment for rangeland uses. The 2.0 lbs a.e./ A is what the registrant stated at the SMART Meeting as the rate they intended to support.

Appendix C: TOLERANCE REASSESSMENT SUMMARY

The established tolerances for dicamba are listed in 40 CFR §180.227. There are three dicamba tolerance expressions. Under 40 CFR §180.227 (a)(1), the tolerances are expressed in terms of the combined residues of the herbicide dicamba (3,6-dichloro-o-anisic acid) and its metabolite 3,6-dichloro-5-hydroxy-o-anisic acid. The tolerances listed in 40 CFR §180.227 (a)(2) are expressed in terms of the combined residues of dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid. Finally, the tolerances listed in 40 CFR §180.227 (a)(3) are expressed in terms of the combined residues of dicamba and its metabolites 3,6-dichloro-5-hydroxy-o-anisic acid and 3,6-dichloro-2-hydroxybenzoic acid.

The results of plant and animal metabolism studies suggest that the various tolerance expressions for dicamba are appropriate. The results of a confined rotational crop study indicate that tolerances need not be established for rotational crops pending label revisions to specify appropriate rotational crop restrictions.

A summary of the tolerance reassessment and recommended modifications in commodity definitions for dicamba is presented in Table C1.

Tolerances Established Under CFR §180.227 (a)(1)

Pending label revisions and/or adjustment of tolerances, there are adequate residue data to reassess the tolerances for: barley, grain, hay, and straw; corn, field, grain, forage, and stover; grass forage and hay; wheat grain, straw, forage and hay; and sorghum grain, forage, and stover.

The submitted data for many commodities do not support the established tolerances because they do not reflect the maximum use rates listed in Dicamba Master Use Profile. To fulfill reregistration requirements, the registrant are required to submit additional data for sugarcane. In lieu of submitting additional data, the registrants are given the option to rely on the available data provided they revise their product labels for consistency with the reviewed data.

HED will allow the translation of available/requested data from some crop commodities to agronomically related commodities with identical uses. Where this situation exists, any HED recommendations with regards to label revision and tolerance reassessment should apply to both crop commodities. The following translations have been made in this Residue Chemistry Chapter: (i) data from field corn grain and stover may be translated to pop corn grain and stover; (ii) data from wheat grain may be translated to proso millet grain and rye grain; (iii) data from wheat forage, hay, and straw may be translated to oat forage, hay, and straw; and (iv) data from wheat straw may be translated to proso millet straw

Pending submission of supporting storage stability data, an acceptable sugarcane processing study is available to reassess the established tolerance for sugarcane molasses. When the maximum HAFT combined residue level (0.183 ppm) of the RAC is multiplied by the observed concentration factor for sugarcane molasses (24.4x), the resulting level is 4.465 ppm which is higher than the current tolerance of 2.0 ppm. Based on these data, HED recommends that the tolerance for sugarcane molasses be increased from 2.0 ppm to 5.0 ppm, toxicological

considerations permitting.

The Agency no longer considers sugarcane forage and fodder to be significant livestock feed items, and these items have been deleted from Table 1 of OPPTS 860.1000. Therefore, the respective tolerances should be revoked.

The generic "corn, forage" tolerance should be revoked since a separate tolerance for field corn forage is established. The generic "corn, stover" tolerance should be revoked since separate tolerances are established for field corn stover and pop corn stover. The generic "corn, grain" tolerance should be split into: "corn, field, grain" and "corn, pop, grain".

Tolerances Needed Under CFR §180.227 (a)(1)

Tolerances are needed for proso millet forage and hay. The available/requested data for wheat forage and hay may be translated to proso millet forage and hay.

Tolerances are needed for rye grain, forage, and straw. The available/requested data for wheat grain, forage, and straw may be translated to rye grain, forage, and straw.

Tolerances Established Under CFR §180.227 (a)(2)

Pending label revisions and/or adjustment of tolerance, there are adequate data to reassess the established tolerance for asparagus.

A ruminant feeding study conducted at a dosing level of 1000 ppm is under review. Assuming this study is adequate sufficient data are available to reassess the established ruminant tolerances.

Tolerances Established Under CFR §180.227 (a)(3)

There are adequate data to reassess the tolerances for soybean seed and soybean hulls.

An acceptable soybean processing study is available to reassess the established tolerance for soybean hulls. When the HAFT combined residue level (7.44 ppm) for the RAC is multiplied by the observed concentration factor for soybean hulls (3.8x), the resulting level is 28.272 ppm which suggests that the existing tolerance of 13.0 ppm needs an upward adjustment. Based on these data, HED recommends that the tolerance for soybean hulls be increased from 13.0 ppm to 30.0 ppm.

There are adequate residue data on the aspirated grain fractions of sorghum, soybean, and wheat and may be translated to corn.

Tolerances That May Be Needed Under CFR §180.227 (a)(3)

It is the current Agency policy to allow label restrictions on the feeding/grazing of livestock animals on soybean forage and hay, thus, precluding the need for residue data and tolerances for these soybean commodities. HED defers to RD for verifying whether such restrictions exist on

product labels. If such restrictions appear on the labels, then residue data and tolerances for soybean forage and hay are not necessary. If no such restrictions appear on the labels, then the registrants are required to propose tolerances for soybean forage and hay; based on the available data, a tolerance level of 0.1 ppm would be appropriate for each soybean commodity. Concomitant with these tolerance proposals, the registrants are required to propose a maximum seasonal rate of 0.5 lb ae/A for preplant application on soybean grown for forage and hay only.

Pending Tolerance Petition:

PP#6E06209: Interregional Research Project No. 4 (IR-4) has submitted a petition, on behalf of the Agricultural Experiment Stations of MN, ND and WI, proposing the following permanent tolerances for the combined residues of the herbicide dicamba and its 5-hydroxy (5-OH) metabolite (3,6-dichloro–5-hydroxy-o-anisic acid) in/on: sweet corn forage at 1.0 ppm, fresh sweet corn at 0.1 ppm, and sweet corn stover at 1.0 ppm. HED's evaluation of residue data and analytical methods (DP Barcode D275611, 7/26/2001, G. Kramer) concluded that additional field residue trials need to be conducted and a revised Section F must be submitted before a favorable recommendation can be made.

Codex/International Harmonization

No Codex MRLs have been established for dicamba; therefore, issues of compatibility between Codex MRLs and U.S. tolerances do not exist. Compatibility cannot be achieved with the Canadian negligible residue limits or with Mexican MRLs because these levels are expressed in terms of parent compound only.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Dicamba Tolerances Listed Under 40 CFR §180.227 (a)(1) [Expressed in terms of the combined residues of dicamba and its metabolite 3,6-dichloro-5-hydroxy-*o*-anisic acid]			
Barley, grain	6.0	6.0	
Barley, hay	2.0	2.0	
Barley, straw	15.0	15.0	
Corn, field, forage	3.0	3.0	The combined residues ranged from <0.01 to 2.27 ppm in/on field corn forage harvested 39-71 days following the last of three sequential treatments for a total of 2.75 lb ae/A. The combined residues ranged from <0.01 to 2.45 ppm in/on field corn fodder harvested 66-123 days following same sequential treatments.
Corn, field, stover	3.0	3.0	
Corn, forage	0.5	Revoke	The generic "corn, forage" tolerance should be revoked since a separate tolerance for field corn forage is established.
Corn, grain	0.5	0.1	The combined residues ranged from <0.01 to 0.015 ppm in/on field corn grain samples harvested 69-123 days following the last of three sequential treatments for a total of 2.75 lb ae/A. The generic "corn, grain" tolerance should be split into: "corn, field, grain"; and "corn, pop, grain".
Corn, pop, stover,	3.0	3.0	HED will allow the translation of available data for field corn stover to pop corn stover. Any label revision for field corn should also be made for pop corn. Concurrently, any adjustment to the field corn stover tolerance should also be applied as necessary to the pop corn stover tolerance.
Corn, stover	0.5	Revoke	The generic "corn, stover" tolerance should be revoked since separate tolerances are established for field corn stover and pop corn stover.
Cotton, undelinted seed	5.0	TBD	
Cotton, meal	5.0	TBD	

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Crop Group 17 (grass forage, fodder, and hay)			The combined residues ranged 66-358 ppm in/on grass forage samples harvested immediately (0-day) following a single application at 2.0 lb ae/A (1x). The combined residues ranged 25-201 ppm in/on grass hay samples harvested 7 days following a single application 1x. Based on these data, HED is reassessing the grass forage tolerance at 400 ppm and the grass hay tolerance at 250 ppm. Concomitant with the reassessment of these tolerances, HED is requesting RD to verify that all dicamba labels specify a 0-day PHI/PGI for grass forage and a 7-day PHI for grass hay when applied at a maximum of 2.0 lb ae/A.
- Grass forage	125.0	400	
- Grass hay	200.0	250	
Millet, proso, grain	0.5	2.0	HED will allow the translation of available/requested data for wheat grain and straw to proso millet grain and straw since the Dicamba Master Use Profile indicates that the application rate of the two crops is identical. Any label revision for wheat should also be made for proso millet. Concurrently, any adjustment to the wheat grain and straw tolerances should also be applied as necessary to the proso millet grain and straw tolerances.
Millet, proso, straw	0.5	TBD	
Oat, grain	0.5	2.0	HED will allow the translation of available/requested data for wheat grain to oat grain since the Dicamba Master Use Profile indicates that the application rate of the two crops is identical.
Oat, forage	80.0	2.0	HED will allow the translation of available/requested data for wheat forage, hay, and straw to oat forage, hay, and straw since the Dicamba Master Use Profile indicates that the application rate of the two crops is identical.
Oat, hay	20.0	TBD	
Oat, straw	0.5	30	
Sorghum, grain	3.0	4.0	The maximum combined residues were 2.73 ppm (MRID 43245203) and 3.164 ppm (MRID 44089306) in/on sorghum grain harvested 30-42 days following sequential treatments for a total rate of 0.5 lb ae/A (1x the maximum rate listed in the Dicamba Master Use Profile). These data suggest that the established tolerance for sorghum grain may be too low. Based on the reviewed data, HED is recommending a tolerance level of 4.0 ppm for sorghum grain concomitant with label revision to specify a 30-day PHI.

Table 9. Tolerance Reassessment Summary for Dicamba.

Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Sorghum, forage	3.0	0.5	The maximum combined residues were 0.46 ppm (MRID 43245203) and 0.350 ppm (MRID 44089306) in/on sorghum forage samples harvested 20-72 days following a single postemergence application at 0.25 lb ae/A (0.5x the seasonal rate listed in the Dicamba Master Use Profile). The maximum combined residues were 8.22 ppm (MRID 43245203) and 4.29 ppm (MRID 44089306) in/on sorghum fodder (stover) samples collected at PHIs of 30-42 days following the last of two applications for a total rate of 0.5 lb ae/A (1x). These data suggest that the established tolerance for sorghum forage may be too high and the tolerance for fodder too low. Based on these data, HED is recommending tolerance levels of 0.5 ppm for sorghum forage and 10.0 ppm for sorghum stover concomitant with the following recommended label revisions: (i) a 20-day PHI and a maximum single/seasonal rate of 0.25 lb ae/A for sorghum forage; and (ii) a 30-day PHI for sorghum fodder (stover) at a maximum seasonal rate of 0.5 lb ae/A.
Sorghum, grain, stover	3.0	10	
Sugarcane, cane	0.1	TBD [1]	The available data do not support the maximum seasonal single/yearly rate of 2.8 lb ae/A that is listed in the Dicamba Master Use Profile because the sugarcane trials were conducted at an application rate of 2.0 lb ae/A. The maximum combined residues were 0.202 ppm in/on sugarcane harvested 87-173 days following a single layby application at 2.0 lb ae/A. The registrants are required to submit additional data on sugarcane reflecting a maximum single/yearly rate of 2.8 lb ae/A. Alternatively, the registrants may rely on the available data provided they are willing to revise their product labels for consistency with the reviewed data. If the registrants elect to choose the latter option, then they will be required to revise product labels to specify a maximum seasonal rate of 2.0 lb ae/A and an 87-day PHI for sugarcane. Based on the reviewed data, the existing tolerance of 0.1 ppm for sugarcane is too low, and HED is recommending that it be reassessed at 0.3 ppm *if* the registrants elect to revise product labels as detailed above.
Sugarcane, fodder	0.1	Revoke	These items are no longer regulated and have been removed from Table 1 of OPPTS 860.1000.
Sugarcane, forage	0.1	Revoke	

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Sugarcane, molasses	2.0	5.0	When the maximum HAFT combined residue level (0.183 ppm) of the RAC is multiplied by the observed concentration factor for sugarcane molasses (24.4x), the resulting level is 4.465 ppm which is higher than the current tolerance of 2.0 ppm. Based on these data, HED recommends that the tolerance for sugarcane molasses be increased from 2.0 ppm to 5.0 ppm, pending submission of supporting storage stability data.
Wheat, forage	80.0	TBD	Additional data are currently under review.
Wheat, grain	2.0	2.0	The combined residues were <0.01 to 0.15 ppm in/on samples of wheat grain harvested 63-125 days following one spring broadcast application at 0.25 lb ae/A. The combined residues were 0.039 to 1.4 ppm in/on grain samples harvested 6-12 days following the last of two treatments for a total of 0.5 lb ae/A.
Wheat, hay	20.0	TBD	Additional data are currently under review.
Wheat, straw	30.0	30.0	The combined residues were 0.011 to 0.97 ppm in/on samples of wheat straw harvested 63-125 days following one spring broadcast application at 0.25 lb ae/A. The combined residues were 0.13 to 26 ppm in/on straw samples harvested 6-12 days following the last of two treatments for a total of 0.5 lb ae/A.
Dicamba Tolerances Needed Under 40 CFR §180.227(a)(1)			
Millet, proso, forage	None	TBD	HED will allow the translation of available/requested data for wheat forage and hay to proso millet forage and hay since the Dicamba Master Use Profile indicates that the application rate for wheat is slightly higher than millet.
Millet, proso, hay	None	TBD	
Rye, grain	None	2.0	HED will allow the translation of available/requested data for wheat grain, forage, and straw to rye grain, forage, and straw since the Dicamba Master Use Profile indicates that the yearly application rate of the two crops is identical.
Rye, forage	None	TBD	
Rye, straw	None	30.0	
Dicamba Tolerances Listed in 40 CFR §180.227 (a)(2) [Expressed in terms of the combined residues of dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid]			
Asparagus	4.0	4.0	Th combined residues ranged 0.28-3.29 ppm in/on asparagus samples harvested 24 hours following a single application at 1x the maximum rate listed in the Dicamba Master Use Profile. These data support the currently established tolerance of 4.0 ppm on asparagus pending verification by RD that the label PHI for asparagus is 24 hours or 1 day.

Table 9. Tolerance Reassessment Summary for Dicamba.

Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Cattle, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Cattle, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Cattle, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Cattle, meat byproducts	0.2	3.0	*Cattle, meat by-products, except kidney.* Reassessed values are based on a new ruminant feeding study currently under review.
Cattle, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Goat, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Goat, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Goat, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Goat, meat byproducts	0.2	3.0	*Goat, meat by-products, except kidney*
Goat, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Hog, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Hog, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Hog, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Hog, meat byproducts	0.2	3.0	*Hog, meat by-products, except kidney*
Hog, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Horse, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Horse, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Horse, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Horse, meat byproducts	0.2	3.0	*Horse, meat by-products, except kidney* Reassessed values are based on a new ruminant feeding study currently under review.
Horse, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Milk	0.3	0.2	Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Sheep, meat byproducts	0.2	3.0	*Sheep, meat by-products, except kidney* Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Dicamba Tolerances Under 40 CFR §180.227(a)(3) [Expressed in terms of the combined residues of dicamba and its metabolites 3,6-dichloro-5-hydroxy-*o*-anisic acid and 3,6-dichloro-2-hydroxybenzoic acid]			
Grain, aspirated grain fractions	5100	1000	There are adequate residue data on the aspirated grain fractions of sorghum, soybean, and wheat, and can be translated to corn.
Soybean, hulls	13.0	30.0	When the maximum HAFT combined residue level (7.44 ppm) of the RAC is multiplied by the observed concentration factor for soybean hulls (3.8x), the resulting level is 28.272 ppm which suggests that the existing tolerance of 13.0 ppm is too low. HED recommends that the tolerance for soybean hulls be increased from 13.0 ppm to 30.0 ppm.
Soybean, seed	10.0	10.0	The highest total residues were 8.13 ppm in/on samples of soybean seed harvested 6-8 days following treatments at 1.25x the maximum rate listed in the Dicamba Master Use Profile.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Dicamba Tolerances That May Be Needed Under 40 CFR §180.227(a)(3)			
Soybean, forage	None	TBD	It is the current Agency policy to allow label restrictions on the feeding/grazing of livestock animals on soybean forage and hay, thus, precluding the need for residue data and tolerances. HED defers to RD for verifying whether such restrictions exist on product labels. If such restrictions appear on the labels, then residue data and tolerances for soybean forage and hay are not necessary. If no such restrictions appear on the labels, then the registrants are required to propose tolerances for soybean forage and hay; based on the available data, a tolerance level of 0.1 ppm would be appropriate for each soybean commodity. Concomitant with these tolerance proposals, the registrants are required to propose a maximum seasonal rate of 0.5 lb ae/A for preplant application on soybean grown for forage and hay.
Soybean, hay	None	TBD	

[1] TBD = To be determined. Additional data/information are required for tolerance reassessment.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: September 13, 2005

MEMORANDUM

SUBJECT: **Dicamba:** HED Chapter of the Reregistration Eligibility Decision Document (RED) - Phase I. PC Code: 029801; DP Barcode: D317720.

Regulatory Action: Phase 1 Reregistration Action
Risk Assessment Type: Single Chemical Aggregate

FROM: Christine Olinger, Risk Assessor
Reregistration Branch I
Health Effects Division (7509C)

AND

Yung Yang, Ph.D., Toxicologist
Timothy Dole, Industrial Hygienist
Monica Hawkins, M.P.H., Environmental Health Scientist
Health Effects Division (7509C)

THROUGH: Whang Phang, Ph.D., Branch Senior Scientist
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TO: Kendra Tyler
Branch
Special Review and Reregistration Division (7508C)

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1.0 Executive Summary

Dicamba (2-methoxy-3,6-dichlorobenzoic acid) is a selective benzoic acid herbicide registered for the control of certain broadleaf weeds and woody plants before their emergence. It is an auxin agonist that is readily translocated symplastically and apoplastically with accumulation in meristemic regions of the plant. Sensitive plants exhibit rapid uncontrolled growth characterized by twisting and curling of stems and petioles, stem elongation and swelling and leaf cupping. Weed control is generally achieved in 5 to 7 days.

Different forms of dicamba (acid and salt) have registered uses on rights of way areas, asparagus, barley, corn (field and pop), grasses grown in pasture and rangeland, oats, proso millet, rye, sorghum, soybeans, sugarcane, and wheat. Application rates range from 0.5 to 2.8 lb ae/A. Residential uses include broadcast and spot treatment on golf courses and lawns.

Dicamba has a low acute toxicity via oral, dermal or inhalation route. It is an eye and dermal irritant but it is not a skin sensitizer. Following oral administration, dicamba is rapidly absorbed and excreted in urine and feces. Consistent neurotoxic signs (e.g., ataxia, decreased motor activity, impaired righting reflex and gait) were observed in many studies in rats and rabbits at high doses. There was an increased incidence of abortion in the rabbit developmental toxicity study at doses that also showed maternal toxicity. In a two-generation reproduction study, offspring toxicity was manifested as decreased pup body weight gain in all generations at a dose lower than the parental systemic toxicity NOAEL. Developmental studies in rats and rabbits showed no evidence (qualitative or quantitative) for increased susceptibility following *in utero* and/or pre-/post-natal exposure of dicamba. Dicamba is classified as **"Not Likely to be Carcinogenic to Humans"** by the oral route. Mutagenicity studies did not demonstrate evidence of mutagenic potential for dicamba although some positive results were reported in published literature.

An acute neurotoxicity study in rats was selected for the general population, including infants and children, for an endpoint of concern for a single oral exposure risk assessment. For the short- and intermediate-term incidental oral exposure and the chronic RfD, a multi-generation reproduction study in rats was selected based on impaired pup growth (decreased pup weights).

The dermal exposure limits for all durations were based on a multi-generation reproduction study in rats. The rat 28-day dermal toxicity study was not selected because the offspring effect in the reproductive study was not measured in this study. In addition, the NOAEL (1000 mg/kg/day) in the 28-day dermal toxicity study would not be protective of the reproductive-offspring effects in the rat multi-generation reproduction study with a NOAEL of 45 mg/kg/day using a dermal absorption factor of 15%. The multi-generation reproduction study with a longer duration and a NOAEL of 45 mg/kg/day will be protective and appropriate for short-, intermediate- and long-term dermal risk assessments. Since an oral NOAEL was selected, a 15% dermal absorption factor was used for route-to-route extrapolation for assessing dermal risk.

The inhalation endpoints selected paralleled the determinations made for the dermal exposure assessments above and assumed a 100% default assumption in the absence of a repeated exposure inhalation toxicity study.

The uncertainty factors used in determining the acute and chronic RfD exposure limit were 100x (10x for intraspecies variation and 10x for interspecies extrapolation). An additional 3x was applied to acute dietary risk assessment for general population for using a LOAEL in establishing the acute reference dose.

Several plant metabolism studies have been submitted for dicamba. Generally there are two major plant metabolites 3,6-dichloro-5-hydroxybenzoic acid (5-OH dicamba) and 3,6-dichlorosalicylic acid (DCSA), which are structurally similar to the parent compound and are included in the dietary risk assessment. The dietary exposure estimates were conducted assuming 100% crop treated and tolerance-level residues in all crops. For the acute and chronic assessments the most highly exposed subgroup was children, ages 1-2. The exposure estimates were well below the levels of concern, with the acute exposure at 5.4% of the acute population adjusted dose (aPAD) and the chronic exposure at 6.5% of the chronic population adjusted dose (cPAD). The actual exposures are likely to be much lower than those estimated in this assessment because of the percent crop treated and residue levels used in this evaluation.

Dicamba could potentially be found in drinking water. Environmental fate studies show that the major environmental degradate would be DCSA. Sufficient drinking water monitoring data from surface water sources were not available so estimated drinking water concentrations (EDWCs) were determined for surface water resources using PRZM-EXAMS. Ground water monitoring data were used for a scoping assessment when ground water could be a source of drinking water. When food and water exposures are aggregated the total dietary exposure for acute and chronic scenarios are well below the level of concern for all population groups.

Exposure to dicamba may occur in residential settings from treatment of turf around the home and at golf courses. Residential handler assessments were conducted for homeowners applying dicamba to lawns using various types of application equipment. Residential post-application assessments were conducted for adults doing yardwork after application or playing golf on treated turf, and were conducted for children playing on a treated lawn or consuming dirt or pesticide granules while playing. Even when exposures occur on the day of treatment, all of the residential exposures are considerably below the level of concern.

The Food Quality Protection Act (FQPA) requires EPA to aggregate or add exposures from food, water, and residential settings. When residential handler or post-application exposures are added to food and water exposures for any exposure duration, the risk estimates are all well below the levels of concern. For example, the scenario with the highest exposure estimate, a child playing on a treated lawn and consuming treated food) produced a margin of exposure (MOE) of 1030; any exposure with an MOE exceeding 100 is considered to be not of concern.

The risks for occupational exposures were estimated for pesticide applicators as well as people who may enter treated fields after application. The MOEs were calculated for short/intermediate term dermal and inhalation exposures using standard assumptions and unit exposure data for a wide range of application methods and equipment. The unit exposure data were taken from the Pesticide Handlers Exposure Database (PHED) and the Outdoor Residential Exposure Task Force (ORETF) studies for professional lawn care operators. All of the mixer/loader MOEs exceed the target of 100 with the single layer personal protective equipment (PPE) and are not of

concern. The MOEs for applicators are above 100 with baseline or single layer PPE . The MOEs for the mixer/loader/applicators are acceptable with single layer PPE and the MOEs for the flaggers are acceptable with baseline PPE. The labels typically require baseline clothing with water proof gloves. There are no residual concerns regarding occupational exposure to dicamba.

2.0 Ingredient Profile

2.1 Summary of Registered/Proposed Uses

Dicamba (2-methoxy-3,6-dichlorobenzoic acid) is a selective benzoic acid herbicide registered for the control of certain broadleaf weeds and woody plants before their emergence. It is an auxin agonist that is readily translocated symplastically and apoplastically with accumulation in meristemic regions of the plant. Sensitive plants exhibit rapid uncontrolled growth characterized by twisting and curling of stems and petioles, stem elongation and swelling and leaf cupping. Weed control is generally achieved in 5 to 7 days.

Different forms of dicamba (acid and salt) have registered uses on rights of way areas, asparagus, barley, corn (field and pop), grasses grown in pasture and rangeland, oats, proso millet, rye, sorghum, soybeans, sugarcane, and wheat. Application rates range from 0.5 to 2.8 lb ae/A. Residential uses include broadcast and spot treatment on golf courses and lawns.

The registrants intend to support all currently registered uses described in the Use Profile, which is provided in Appendix B of this document. The different forms of dicamba acid and salts that will be supported for reregistration, include: the dicamba acid (PC Code 029801), dimethylamine (DMA) salt (PC Code 029802), sodium (Na) salt (PC Code 029806), isopropylamine (IPA) salt (PC Code 128944), diglycolamine (DGA) salt (PC Code 128931), and potassium (K) salt (PC Code 129043).

There were approximately 434 active products of Dicamba formulated from 6 different forms. The acid, dimethylamine and sodium salt ester forms of Dicamba have the most products. The products are formulated as liquids, standard granules and water dispersible granules. The residential products are typically formulated as granular weed and feed formulations or as liquids in concentrates or ready to use sprays.

2.2 Structure and Nomenclature

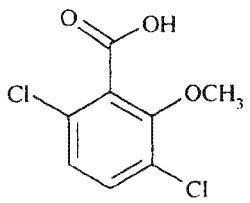
TABLE 2.1. Dicamba and its Salts Nomenclature	
PC Code 029801	
Chemical structure	

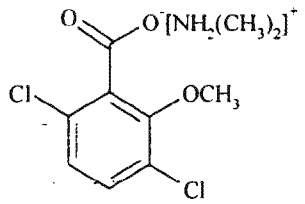
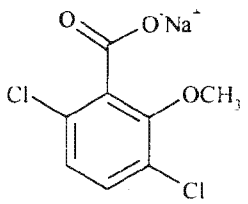
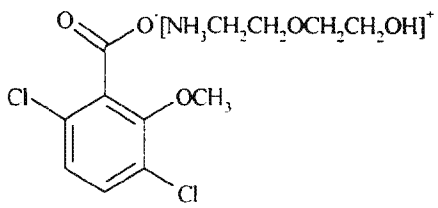
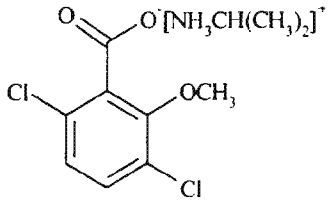
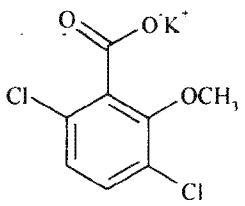
TABLE 2.1. Dicamba and its Salts Nomenclature	
Common name	Dicamba acid
Molecular Formula	$C_8H_6Cl_2O_3$
Molecular Weight	221.04
IUPAC name	3,6-dichloro-*o*-anisic acid
CAS name	3,6-dichloro-2-methoxybenzoic acid or 2-methoxy-3,6-dichlorobenzoic acid
CAS #	1918-00-9
PC Code 029802	
Chemical structure	
Common name	Dicamba dimethylamine salt (DMA salt)
Molecular Formula	$C_{10}H_{13}Cl_2NO_3$
Molecular Weight	266.1
CAS #	2300-66-5
PC Code 029806	
Chemical structure	
Common name	Dicamba sodium salt (Na salt)
Molecular Formula	$C_8H_5Cl_2NaO_3$
Molecular Weight	243.0
CAS #	1982-69-0
PC Code 128931	
Chemical structure	
Common name	Dicamba diglycolamine salt (DGA salt)
Molecular Formula	$C_{12}H_{17}Cl_2NO_5$
Molecular Weight	326.18
CAS #	104040-79-1
PC Code 128944	

TABLE 2.1. Dicamba and its Salts Nomenclature	
Chemical structure	
Common name	Dicamba isopropylamine salt (IPA salt)
Molecular Formula	$C_{11}H_{15}Cl_2NO_3$
Molecular Weight	280.15
CAS #	55871-02-8
PC Code 129043	
Chemical structure	
Common name	Dicamba potassium salt (K salt)
Molecular Formula	$C_8H_5Cl_2KO_3$
Molecular Weight	259.1
CAS #	10007-85-9

2.3 Physical and Chemical Properties

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Dicamba acid (PC Code 029801)		
Melting point	114-116 °C (PAI) 90-100 °C (87% TGAI)	SRR Reregistration Standard, 6/30/89
pH	2.5-3.0 (87% TGAI)	
Density, bulk density, or specific gravity	1.57 g/mL at 25 °C (87% TGAI)	
Water solubility	0.5 g/100 mL at 25 °C (PAI)	
Solvent solubility	g/100 mL at 25 °C (PAI) dioxane 118.0 ethanol 92.2 isopropyl alcohol 76.0 methylene chloride 26.0 acetone 17.0 toluene 13.0 xylene 7.8 heavy aromatic naphthalene 5.2	

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Vapor pressure	3.4 x 10^{-5} mm Hg at 25 °C (PAI)	
Dissociation constant, pK_a	1.97 (PAI)	
Octanol/water partition coefficient	0.1 (PAI)	
UV/visible absorption spectrum	neutral: 511 (275 nm) acidic (pH 0-1): 1053 (281 nm) basic (pH 13-14): 469 (274 nm)	RD D266167, 6/26/00, B. Kitchens
Dicamba DMA salt (PC Code 029802)		
Melting point	101.0-114.5 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	3.89 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.77 g/mL at 25 °C (tap density)	
Water solubility	94.5 g/100 mL at 25 °C	
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	D198000, 5/5/94, P. Deschamp
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	K_{OW} = 0.078	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
UV/visible absorption spectrum	**Not available**	
Dicamba Na salt (PC Code 029806)		
Melting point	320-325 °C	RD Memorandum, 9/26/94, T. Alston
pH	7.16	
Density, bulk density, or specific gravity	1.03 g/mL at 25 °C	
Water solubility	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the Na salt	D198000, 5/5/94, P. Deschamp
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the Na salt	
UV/visible absorption spectrum	**Not available**	
Dicamba DGA salt (PC Code 128931)		

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Melting point	52.0-85.0 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	7.60 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.69 g/mL at 25 °C (tap density)	
Water solubility	107 g/100 mL at 25 °C	
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	D198000, 5/5/94, P. Deschamp
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	K_{ow} = 0.061	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
UV/visible absorption spectrum	**Not available**	
Dicamba IPA salt (PC Code 128944)		
Melting point	93.5-127.5 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	4.68 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.63 g/mL at 25 °C (tap density)	
Water solubility	59.6 g/100 mL at 25 °C	
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	D198000, 5/5/94, P. Deschamp
Vapor pressure		
Dissociation constant, pK_a		
Octanol/water partition coefficient	K_{ow} = 0.070	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
UV/visible absorption spectrum	**Not available**	
Dicamba K salt (PC Code 129043)		
Melting point	Decomposes at 213.5 °C	D213276, D216855, D216859, D216853, D216857, D216862, D217061, D218789, D218792, D218784, D218787, and D218786, 11/21/95, L. Cheng
pH	8.12 at 25 °C (1% solution)	
Density, bulk density, or specific gravity	0.88 g/mL at 25 °C (tap density)	
Water solubility	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the K salt	D198000, 5/5/94, P. Deschamp
Solvent solubility	N/A; data for the free acid are representative of the dicamba salts	
Vapor pressure		

TABLE 2.2. Physicochemical Properties of Dicamba and its Salts		
Parameter	Value	Reference
Dissociation constant, pK_a		
Octanol/water partition coefficient	N/A; data for the organic salts (DMA, DGA, and IPA) are representative of the K salt	
UV/visible absorption spectrum	**Not available**	

3.0 Hazard Characterization/Assessment

3.1 Hazard and Dose-Response Characterization

Dicamba has a low acute toxicity via oral, dermal or inhalation route. It is an eye and dermal irritant but it is not a skin sensitizer. Following oral administration, dicamba is rapidly absorbed and excreted in urine and feces without significant metabolism. Dogs are generally considered to be toxicologically more sensitive when exposed to dicamba. However, a submitted toxicity study in dogs showed that no effect was seen at the highest dose tested (52 mg/kg/day) which indicated that the animals in the study were not tested at high enough doses. Consistent neurotoxic signs (e.g., ataxia, decreased motor activity, impaired righting reflex and gait) were observed in many studies in rats and rabbits at high doses. There is an increased incidence of abortion in the rabbit developmental toxicity study at doses that also showed maternal toxicity. In a two-generation reproduction study, offspring toxicity was manifested as decreases in pup weight in all generations at a dose lower than the parental systemic toxicity NOAEL. Developmental studies in rats and rabbits showed no evidence (qualitative or quantitative) for increased susceptibility following *in utero* and/or pre-/post-natal exposure of dicamba. Dicamba is classified as **"Not Likely to be Carcinogenic to Humans"** by the oral route. Mutagenicity studies did not demonstrate evidence of mutagenic potential for dicamba although some positive results were reported in published literature.

An acute neurotoxicity study in rats was selected for the general population, including infants and children, for an endpoint of concern for a single oral exposure risk assessment. For the short- and intermediate-term incidental oral exposure and the chronic RfD, a multi-generation reproduction study in rats was selected based on impaired pup growth (decreased pup weights).

The dermal exposure limits for all durations were based on a multi-generation reproduction study in rats. The rat 28-day dermal toxicity study was not selected because the offspring effect in the reproductive study was not measured in this study. In addition, the NOAEL (1000 mg/kg/day) in the 28-day dermal toxicity study would not be protective of the reproductive-offspring effects in the rat multi-generation reproduction study with a NOAEL of 45 mg/kg/day using a dermal absorption factor of 15%. The multi-generation reproduction study with a longer duration and a NOAEL of 45 mg/kg/day will be protective and appropriate for short-, intermediate- and long-term dermal risk assessments. Since an oral NOAEL was selected, a 15% dermal absorption factor was used for route-to-route extrapolation.

The inhalation endpoints selected paralleled the determinations made for the dermal exposure assessments above and assumed a 100% default relative inhalation to oral absorption assumption in the absence of a repeated exposure inhalation toxicity study.

The uncertainty factors used in determining the acute and chronic RfD exposure limit were 100x (10x for intraspecies variation and 10x for interspecies extrapolation). An additional 3x was applied to acute dietary risk assessment for general population for using a LOAEL because most of the clinical signs of neurotoxicity were seen at repeated doses of 150 mg/kg/day or above (TXR No. 0050280).

Note that a profile of the acute toxicity studies may be found in Table 3.1 and other studies may be found in Table 3.2.

3.2 Absorption, Distribution, Metabolism, Excretion (ADME)

Multiple studies describing the metabolism or the pharmacokinetic of dicamba in rats have been submitted to the Agency. The metabolism study in rats showed that following oral administration, dicamba is rapidly absorbed and excreted. Over 95% is excreted in the urine and the compound is not metabolized or accumulated by the tissues.

The plasma pharmacokinetic studies in rats showed that absorption of the radiolabeled dicamba was rapid, with peak plasma concentrations found within 2 hours of treatment. Absorption was not saturated, even at the highest dose, as indicated by increasing plasma concentrations with doses. However, the increase in plasma concentration was non-linear and disproportionate from one dose to the next doses, which is consistent with saturation of excretion. No significant treatment-related differences between the sexes or time of radiolabel administration were found. Another plasma pharmacokinetic study suggested that dicamba acts as an inhibitor of renal anion transport.

Table 3.1. Acute Toxicity Profile on Dicamba

OPPTS Guideline	Study Type	MRID	Results	Toxicity Category
870.1100	Acute oral toxicity / rat	00078444	LD_{50} => 2740 mg/kg	III
870.1200	Acute dermal toxicity / rat	00241584	LD_{50} => 2000 mg/kg	III
870.1300	Acute inhalation toxicity / rat	00263861	LC_{50} => 5.3 mg/L	IV
870.2400	Primary eye irritation / rabbit	00241584	Irritant	II

Table 3.1. Acute Toxicity Profile on Dicamba				
870.2500	Primary dermal irritation / rabbit	00237955	Irritant	II
870.2600	Dermal sensitization / guinea pig	00263861	Non-Sensitizer	--

Table 3.2. Subchronic, Chronic and Other Toxicity Profile for Dicamba		
Guideline No./ Study Type/	**MRID Nos. Doses/Classification**	**Results**
870.3100 Subchronic Oral - Rat	44623101 (1997) (0, 500, 3000, 6000, 12000 ppm) M:0,40.1,238.7,479.4,1000 mg/kg/day F:0,43.2,266.4,535.6,1065.3 mg/kg/day Acceptable/Guideline	NOAEL= 479.4/535.6 mg/kg/day(M/F). LOAEL= 1000/1065.3 mg/kg/day (M/F) based on clinical signs, decr. body weight gains, incr. liver wt and incr. centrolobular hepatocyte hypertrophy and hepatocellular pigmentation.
870.3200 28-Day dermal toxicity - Rat	45814501 (2002) 0,30,300,1000 mg/kg/day (M/F) Acceptable/Guideline	NOAEL= 1000 mg/kg/day (HDT) LOAEL= not determined.
870.3700a Prenatal developmental - Rat	00084024 (1981) 0,64,160,400 mg/kg/day (GD 6-19) Acceptable/Guideline	**Maternal**: NOAEL= 160 mg/kg/day; LOAEL= 400 mg/kg/day based on Incr. mortality, clinical signs, decr. body weight gains, decr. food consumption. **Developmental**: NOAEL= 400 mg/kg/day (HDT), LOAEL not established.
870.3700b Prenatal developmental - NZW Rabbit	42429401 (1992) 0,30,150,300 mg/kg/day (GD 6-18) Range-finding: 0.62.5,125,250.500 mg/kg/day (GD 6-18) Acceptable/Guideline	**Maternal**: NOAEL= 62.5 mg/kg/day, LOAEL= 150 mg/kg/day based on incr. abortion, clinical signs (decr. motor activity, ataxia). **Developmental**: NOAEL= 62.5 mg/kg/day, LOAEL= 150 mg/kg/day based on incr. abortion.
870.3800 Reproduction and fertility effects - Rat	43137101 (1993) (0,500,1500,5000 ppm) M: 0,40,122,419 mg/kg/day F: 0,45, 136, 450 mg/kg/day Acceptable/Guideline	**Parental/Systemic:** NOAEL= 122/136 mg/kg/day (M/F); LOAEL= 419/450 mg/kg/day (M/F) based on clinical signs (slow righting reflex). **Reproductive:** NOAEL=122 mg/kg/day; LOAEL= 419 mg/kg/day based on delayed sexual maturation in F1 males. **Offspring:** NOAEL=45 mg/kg/day; LOAEL= 136 mg/kg/day based on impaired pup growth (decr. pup weights) in all generations during lactation period.
870.4200a Chronic Toxicity/ Carcinogenicity -Rat	00146150 (1985) (0,50,250,2500 ppm) M: 0,2,11,107 mg/kg/day F: 0,3,13,127 mg/kg/day Acceptable/Guideline	NOAEL= 107/127 mg/kg/day (M/F), LOAEL was not established. Not carcinogenic. The study is considered adequate for evaluating the carcinogenic potential.

Table 3.2. Subchronic, Chronic and Other Toxicity Profile for Dicamba

Guideline No./ Study Type/	MRID Nos. Doses/Classification	Results
870.4100b Chronic toxicity - dog	40321102 (1986) (0,100,500,2500 ppm) 0,2,11,52 mg/kg/day Acceptable/Guideline	NOAEL=52 mg/kg/day (HDT).
870.4200b Carcinogenicity - mouse	40872401 (1988) (0,50,150,1000,3000 ppm) M: 0,5.5,17.2,108,358 mg/kg/day F: 0,5.8,18.8,121,354 mg/kg/day Acceptable/Guideline	NOAEL=358/354 mg/kg/day (M/F), LOAEL was not established. Not carcinogenic. The study is considered adequate for evaluating the carcinogenic potential.
870.5100 Gene Mutation Salmonella typhimurium	00143001(1979) Acceptable/Guideline	Not mutagenic.
870.5395 Chromosome aberration (CHO)	40321101 (1986) Acceptable/Guideline	Chromosome aberrations were not induced in a cultured CHO cells at concentrations of 2330, 1170, 590, and 300 µg/mL either with or without S-9 activation.
870.5550 Unscheduled DNA synthesis (UDS)	00143001 (1979) Acceptable/Guideline	No evidence of UDS at levels 0.1 to 3000 µg/mL.
870.6200 Acute Neurotoxicity - Rat	42774104 (1993) 0,300,600,1200 mg/kg Acceptable/Guideline	NOAEL was not established. LOAEL=300 mg/kg based on severe neurologic signs (impaired respiration, rigidity upon handling, prodding, or dropping, impaired gait and righting reflex in both sexes.
870.6200 Subchronic neurotoxicity - Rat	43245210 (1994) (0,3000,6000,12000 ppm) M:0,197.1,401.4,767.9 mg/kg/day F: 0,253.4,472.0,1028.9 mg/kg/day Acceptable/Guideline	NOAEL= 401.4/472.0 mg/kg/day (M/F); LOAEL= 767.9/1028.9 mg/kg/day (M/F) based on rigidity body tone, slightly impaired righting reflex and gait.
870.6300 Developmental Neurotoxicity -Rat	Data Gap	Not available.
870.7485 Metabolism	00028261(1967) Acceptable/guideline	Rapidly absorbed and excreted in urine and feces. Dicamba is not metabolized or bioaccumulation.

3.3 FQPA Considerations

The database is adequate in terms of endpoint studies and dose response information to select appropriate endpoints for prenatal or postnatal risk for infants and children. There is no evidence (qualitative or quantitative) of increased susceptibility following *in utero* and/or pre-natal exposure in the developmental toxicity studies in rats and rabbits. There was evidence of increased sensitivity to the offspring following pre- and/or postnatal exposure in the two-generation reproduction study in rats. In that study, offspring toxicity was manifested as decreased pup body weight in all generations at a dose lower than the parental systemic toxicity NOAEL. However, the degree of concern is low for the quantitative susceptibility because the risk assessment was based on the very same effect seen in the pups with a definitive NOAEL. There are no concern or residual uncertainties for pre- and postnatal toxicity.

After considering the available toxicity data, the risk assessment team determined that a developmental neurotoxicity study (DNT) is not required based on the following reasons: (1) although clinical signs of neurotoxicity were seen in pregnant animals, no evidence of developmental anomalies of the fetal nervous system were observed in the prenatal developmental toxicity studies, in either rats or rabbits, at maternally toxic doses up to 300 or 400 mg/kg/day, respectively; (2) there were no evidence of behavioral or neurological effects on the offspring in the two-generation reproduction study in rats; (3) the ventricular dilation of the brain in the chronic toxicity study was only observed in females at the high dose after two years exposure. The significance of this observation is questionable since no similar histopathological finding was seen in the subchronic neurotoxicity study. In addition, the dicamba risk assessment team evaluated the quality of the exposure data: and, based on these data, recommended that the special FQPA SF be reduced to 1x.

3.3.1 Adequacy of the Toxicity Data Base

The following studies are available in the toxicity database:

- Developmental toxicity studies in rats and rabbits (acceptable).
- Two generation reproduction study in rats (acceptable).
- Acute and subchronic neurotoxicity studies in rats (acceptable).

3.3.2 Evidence of Neurotoxicity

There is evidence of neurotoxicity resulting from exposure to dicamba. The velevant findings are summarized below and the executive summaries of studies are presented in Appendix A.

In the acute neurotoxicity study, at 300 mg/kg bw or above, clinical signes of neurotoxicity consisted of impaired gait and righting reflex, decreased arousal and rears/minutes, and rigidity upon handling were found. At higher dose levels, the effects were more pronounced with additional effects. The subchronic neurotoxicity study in rats showed rigid body tone, impaired righting reflex and gait at 768 mg/kg.

In the developmental toxicity studies in rats ataxia, stiffening of the body when touched, and decreased motor activity were seen at 400 mg/kg in the dams. The developmental toxicity study in rabbits showed that at 150 mg/kg the dams presented signs of ataxia, rales and decreased motor

activity.

A two generation reproduction study demonstrated tense/stiff body tone and slow righting reflex in the dams from both generations at approximately 450 mg/kg. It should be noted that the signs of neurotoxicity were consistent across several studies.

3.3.3 Developmental Toxicity Studies

In a developmental toxicity study (MRID No. 00084024), pregnant (CD Charles River) rats (25/dose group) received gavage administration of dicamba (85.3%) in corn oil at dose levels of 0, 64, 160, or 400 mg/kg/day during gestation days 6 through 19. Maternal toxicity limited to the high dose (400 mg/kg/day) was characterized by mortality in three gravid and one non-gravid dams that exhibited neurotoxic signs prior to death; clinical signs of nervous system toxicity that included ataxia, salivation, stiffening of the body when held, and decreased motor activity; statistically significant ($p<0.05$) decreases in body weight gain during the dosing period; and concomitant decreases in food consumption. Dicamba had no effect on any of the cesarean parameters. For maternal toxicity, the NOAEL was 160 mg/kg/day and the LOAEL was 400 mg/kg/day based on mortality, clinical signs, body weight changes and decreases in food consumption. No Treatment-related fetal gross external, skeletal or visceral anomalies (malformations or variations) were seen at any dose level. For developmental toxicity, the NOAEL was >400 mg/kg/day; a LOAEL was not established. This study is classified **acceptable/guideline** (OPPTS 870.3700a) and satisfies the requirements for a developmental toxicity study in the rat.

In a developmental toxicity study (MRID No. 42429401), inseminated New Zealand White rabbit (19-20/dose) were given oral capsules containing dicamba (90.5%) at dose levels of 0, 30, 150, or 300 mg/kg/day from days 6 through 18 of gestation. No maternal or developmental toxicity was observed at 30 mg/kg/day. At 150 mg/kg/day, maternal toxicity was characterized by abortion (5%) and clinical signs such as ataxia, rales, decreased motor activity. At 300 mg/kg/day maternal toxicity was manifested by abortions (20%), clinical signs, decreased body weight and body weight gain and food consumption. Developmental toxicity at 300 mg/kg/day was manifested by irregular ossification of the nasal bones of the skull. At 150 mg/kg/day, increased incidence of abortion was observed and was considered developmental toxicity. In a range-finding study, NZW rabbits were dosed at 0, 62.5, 125, 250, or 500 mg/kg/day from days 6 through 18 of gestation. No maternal or developmental toxicity was observed at 62.5 mg/kg/day. Treatment-related maternal toxicity was manifested by mortality, increased resorptions and reduction in the litter size at 500 mg/kg/day. Clinical signs occurred at 125, 250, and 500 mg/kg/day. Cesarean sections revealed no treatment-related differences between treated and control groups, and no external malformation or variations were seen in any of the fetuses of the treated does. Based on the results of these studies, the NOAEL for maternal toxicity was 62.5 mg/kg/day and the LOAEL was 150 mg/kg/day based on increased incidences of abortion and clinical signs (i.e., decreased motor activity, ataxia). For developmental toxicity, the NOAEL was 62.5 mg/kg/day and the LOAEL was 150 mg/kg/day based on increased incidence of abortion. This study is classified **acceptable/guideline** (OPPTS 870.3700b; OECD 414) and satisfies the requirements for a developmental toxicity study in the rabbit.

3.3.4 Reproductive Toxicity Study

In a two-generation reproduction study (MRID 43137101), Sprague-Dawley rats (32 or 28/group) received dicamba technical (86.5%) in the diet at dose levels of 0, 500, 1500, or 5000 ppm (0, 40, 122, or 419 mg/kg/day for males and 0, 45, 136 or 450 mg/kg/day for females, respectively) for two generations. Systemic toxicity was observed at 5000 ppm, manifested as clinical signs in dams from both generations during lactation (tense/stiff body tone and slow righting reflex) and significantly increased relative liver to body weights (112% of control) in both generations and sexes, adults as well as weanlings. The increase (107%) in relative kidney weights observed at 1500 and/or 5000 ppm were not considered to be toxicologically significant due to lack of corroborative gross or histopathological lesions in the kidneys. Sexual maturation among male pups in the F1 generation was significantly delayed at 5000 ppm. Similar effects were not seen in females. Significantly decreased pup body weights were observed in all generations and matings at 1500 ppm (86 - 90% of control) and at 5000 ppm (74 - 94% of control) throughout lactation. For parental systemic toxicity, the NOAEL was 122 and 136 mg/kg/day for males and females, respectively, and the LOAEL was 419 and 450 mg/kg/day in males and females based on clinical signs of neurotoxicity. For reproductive toxicity, the NOAEL was 122 mg/kg/day and the LOAEL was 419 mg/kg/day based on delayed sexual maturation in F_1 males. For offspring toxicity, the NOAEL was 45 mg/kg/day and the LOAEL was 136 mg/kg/day based on decreased pup body weight. This study is classified as **acceptable/guideline** and satisfies the guideline requirements (OPPTS 870.3800; OECD 416) for a two-generation reproduction study in the rat.

3.3.5 Additional Information from Literature Sources

No additional relevant toxicity studies from published literature were identified.

3.3.6 Pre-and/or Postnatal Toxicity

3.3.6.1 Determination of Susceptibility

There is no evidence of increased qualitative or quantitative susceptibility following *in utero* and/or pre-natal exposure in the developmental toxicities in rats and rabbits. There was evidence of increased quantitative susceptibility to the offspring following pre- and/or postnatal exposure in the two-generation reproduction study in rats. In that study, offspring toxicity was manifested as decreased pup body weight gain in all generations at a dose lower than the parental systemic toxicity NOAEL. However, the NOAEL of 45 mg/kg/day identified in this study was chosen for risk assessments for all routes and exposure durations other than acute oral exposures. Since this NOAEL is the lowest (most sensitive endpoint) in the dicamba toxicity data base, and the dose-response observed in the study is well defined assuring that this dose is a clear NOAEL, use of the NOAEL and endpoint for risk assessment is protective for all observed toxic effects of the chemical. Therefore, there is low concern for the increased susceptibility observed in the reproduction study since all appropriate risk assessments utilize this endpoint. Additionally, there is no increased susceptibility observed in the developmental toxicity studies. Since the most sensitive observed developmental endpoint (increased incidence of abortion) and the associated NOAEL was used for acute dietary risk assessment for females of child-bearing age, the risk assessment is protective for potential acute toxicity to developing fetuses.

3.3.6.2 Degree of Concern Analysis and Residual Uncertainties

The degree of concern is low for the quantitative susceptibility because the risk assessment was based on the most sensitive endpoint with a definitive NOAEL. There are no concern or residual uncertainties for pre- and postnatal toxicity.

3.3.7 Recommendation for a Developmental Neurotoxicity Study

After considering the available toxicity data, the risk assessment team determined that a developmental neurotoxicity study (DNT) is not required based on the following reasons: (1) although clinical signs of neurotoxicity were seen in pregnant animals, no evidence of developmental anomalies of the fetal nervous system were observed in the prenatal developmental toxicity studies, in either rats or rabbits, at maternally toxic doses up to 300 or 400 mg/kg/day, respectively; (2) there were no evidence of behavioral or neurological effects on the offspring in the two-generation reproduction study in rats; (3) the ventricular dilation of the brain in the chronic toxicity study was only observed in females at the high dose after two years exposure. The significance of this observation is questionable since no similar histopathological finding was seen in the subchronic neurotoxicity study.

3.4 Safety Factor for Infants and Children

3.4.1 Adequacy of the Exposure Data Base

The dietary exposure assessment is based on the exaggerated exposure assumptions, that all crops consumed in the U.S. are treated, and that the commodities bear tolerance level residues. The residential exposure assessment assumes maximum label use rate as well as other conservative assumptions. Therefore, the Agency does not believe that exposure to dicamba will be underestimated.

3.4.2 Conclusion

Based on the hazard data, there are no concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity. In addition, the dicamba risk assessment team evaluated the quality of the exposure data and has no residual uncertainties. Therefore, the team has recommended that the special FQPA Safety Factor be reduced to 1x.

3.5 Hazard Identification and Toxicity Endpoint Selection

A summary of the endpoints and doses selected for risk assessment may be found in Table 3.4 at the end of this section.

3.5.1 Acute Reference Dose (aRfD) - Females age 13-49

No study was identified that demonstrated effects to the developing fetus as a result of a single exposure via the oral route. Therefore, this risk assessment is not required.

3.5.2 Acute Reference Dose (aRfD) - General Population

The results of the Acute Neurotoxicity Study (ACN) in Rats (MRID No.: 42774104) were considered for this endpoint. A summary may be found in Appendix A. The effects observed in this study can be attributed to a single dose and is appropriate for all populations. Neurotoxicity was seen in both sexes at the lowest dose tested, 300 mg/kg/day. With the exception of the decrease in forelimb grip strength, which persisted until day 7, the other neurologic signs such as impaired gaits and righting reflex were seen on the day of dosing. A comparison with the rat developmental toxicity study that had similar clinical signs with a NOAEL of 160 mg/kg/day after 10 days of treatment indicates that the NOAEL for the acute neurotoxicity study is unlikely to be more than 3-fold lower than the LOAEL (ACN LOAEL/3 = 100 mg/kg; rat developmental study NOAEL = 160 mg/kg). Therefore, it was determined that an uncertainty factor of 3 for extrapolation of LOAEL to NOAEL was adequate. The total uncertainty factor is 300x, 10x for interspecies extrapolation, 10x for intraspecies variations, and 3x for using a LOAEL. The acute population adjusted dose for the general population is equal to the acute reference dose and is 1.0 mg/kg/day.

3.5.3 Chronic Reference Dose (cRfD)

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was used for establishing the chronic reference dose. The selected dose and endpoints are appropriate for the route and duration of exposure and is protective of the general population. A summary of this study may found in Section 3.3.4. The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL). An uncertainty factor of 100x is to be applied including 10x for interspecies extrapolation and 10x for intraspecies variations. The chronic population adjusted dose (cPAD) is equal to the chronic reference dose and is 0.45 mg/kg/day.

3.5.4 Incidental Oral Exposure (Short and Intermediate Term)

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was selected for this risk assessment. This study is of the appropriate route and duration of exposure, since effects in the pups were seen on lactation day 21 in both F_2 litters and is protective of the population of concern (infants and children). A summary of this study may found in Section 3.3.4. The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL). An uncertainty factor of 100x is to be applied including 10x for interspecies extrapolation and 10x for intraspecies variations. The chronic population adjusted dose (cPAD) is equal to the chronic reference dose and is 0.45 mg/kg/day.

3.5.5 Dermal Absorption

A dermal absorption study is not available. An upper-bound estimate of dermal absorption was estimated using the NOAEL of 1000 mg/kg/day in the 21-day dermal toxicity rabbit study and the LOAEL of 150 mg/kg/day in the rabbit oral developmental study.

$$\frac{150}{1000} \times 100 = 15\ \%\ \text{dermal absorption factor}$$

3.5.6 Dermal Exposure

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was selected for this endpoint. A summary of this study may found in Section 3.3.4. Although a rat 28-day dermal toxicity study was available which showing no systemic toxicity at the highest dose tested of 1000 mg/kg/day, this dermal study did not assess reproductive and offspring effects. Offspring toxicity in the rat oral multi-generation reproduction study was noted below dosages where parental toxicity was evident. In order to be protective of these effects in the absence of any route-specific data, the reproduction study was chosen for all time periods of exposure, including short-term, since effects in the pups were seen on lactation day 21 in both F_2 litters. Since an oral NOAEL was selected, 15% dermal absorption factor should be used for route-to-route extrapolation. The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL).

3.5.7 Inhalation Exposure

The Multi-generation Reproduction Study in Rats (MRID No.: 43137101) was used for selecting this endpoint. A summary of this study may found in Section 3.3.4. In the absence of a repeated exposure inhalation study, an oral study is employed. Inhalation absorption is assumed to be equivalent to oral (i.e., 100%). The NOAEL for offspring toxicity was 45 mg/kg/day based upon the impaired pup growth (decreased pup weights) at 136 mg/kg/day (LOAEL).

3.5.8 Level of Concern for Margin of Exposure

The levels of concern for occupational and residential exposures are summarized in Table 3.3. For **Occupational Exposure** a margin of exposure (MOE) MOE of 100 is required for short-, intermediate-, and long-term occupational risk assessments for both dermal and inhalation routes of exposure. The MOEs for dermal and inhalation exposures may be combined for occupational exposure risk assessment because the toxicity endpoints for these routes of exposure are the same. For **Residential Exposure** a margin of exposure (MOE) of 100 is required for short-, intermediate-, and long-term residential risk assessments for both dermal and inhalation routes of exposure, and an MOE of 300 is required for acute exposures.

Table 3.3. Summary of Target Margins of Exposure (MOEs) for Risk Assessment				
Route	**Duration**			
	Acute (1 day)	**Short-Term (1-30 Days)**	**Intermediate-Term (1 - 6 Months)**	**Long-Term (> 6 Months)**
Occupational (Worker) Exposure				
Dermal	NA	100	100	100
Inhalation	NA	100	100	100
Residential (Non-Dietary) Exposure				
Oral	300	100	100	N/A
Dermal	300	100	100	100
Inhalation	300	100	100	100
N/A = Not Applicable				

3.5.9 Recommendation for Aggregate Exposure Risk Assessments

A common toxicological endpoint (decreased pup growth) of concern was identified for the short-, intermediate- and long-term durations via the oral, dermal (oral equivalent) and inhalation (oral equivalent) routes. Therefore, the aggregate exposure risk assessment should include oral, dermal and inhalation routes appropriate to the population of concern.

3.5.10 Classification of Carcinogenic Potential

In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), dicamba is classified as "**Not Likely to be Carcinogenic to Humans**". This was based on negative cancer studies in rats and mice which were tested at adequate dose levels to assess the carcinogenicity of dicamba (TXR No. 0053647). A detailed discussion of the carcinogenicity studies may be found in Appendix A of this document.

Table 3.4 Summary of Toxicology Endpoint Selection for Dicamba			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (General population including infants and children	LOAEL = 300 mg/kg/day UF = **300** **Acute RfD** = 1 mg/kg/day	FQPA SF = 1X **aPAD** = acute RfD / FQPA SF = 1.0 mg/kg/day	**Acute Neurotoxicity Study in Rats** LOAEL = **300** mg/kg/day (LDT) based on clinical signs of neurotoxicity.

Table 3.4 Summary of Toxicology Endpoint Selection for Dicamba			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Chronic Dietary (All populations)	NOAEL= **45** mg/kg/day UF = **100** **Chronic RfD** = 0.45 mg/kg/day	FQPA SF = 1X **cPAD** = chronic RfD / FQPA SF = 0.45 mg/kg/day	**Multi-generation Reproduction Study in Rats** LOAEL=136 mg/kg/day based on impaired pup growth (decreased pup weights).
Short-Term Incidental Oral (1 - 30 Days)	Oral NOAEL= 45 mg/kg/day	**Residential** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Intermediate-Term Incidental Oral (1 - 6 Months)	Oral NOAEL= 45 mg/kg/day	**Residential** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Short-Term Dermal (1 - 30 days)	Oral NOAEL= 45 mg/kg/day (Dermal absorption rate = 15%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Intermediate-Term Dermal (1 - 6 Months)	Oral NOAEL= 45 mg/kg/day (Dermal absorption rate = 15%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Long-Term Dermal (> 6 Months)	Oral NOAEL= 45 mg/kg/day (Dermal absorption rate= 15%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Short-Term Inhalation (1 - 30 days)	Oral NOAEL= 45 mg/kg/day (Inhalation absorption rate= 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Intermediate-Term Inhalation (1 - 6 Months)	Oral NOAEL= 45 mg/kg/day (Inhalation absorption rate= 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section

Table 3.4 Summary of Toxicology Endpoint Selection for Dicamba			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Long-Term Inhalation (>6 Months)	Oral NOAEL= 45 mg/kg/day (Inhalation absorption rate= 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Multi-generation Reproduction Study in Rats** See above section
Cancer (Oral, dermal, inhalation)	**Not Likely to be Carcinogenic to human.**		

3.6 Endocrine disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP). While delayed sexual maturation in females was observed in the rat reproduction study, no effects clearly related to endocrine disruption were seen in the toxicity data base.

When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, dicamba may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

4.0 Public Health and Pesticide Epidemiology Data

4.1 Incident Reports

The OPP Incident Data System (IDS), California Department of Pesticide Regulation, National Pesticide Information Center (NPIC), National Institute of Occupational Safety and Health's Sentinel Event Notification System for Occupational Risks (NIOSH SENSOR), and Poison Control Centers

were reviewed for adverse incidents as a result of dicamba exposure. Dicamba is rarely used as a herbicide by itself. Most often it is mixed with other ingredients, particularly other chlorophenoxy herbicides, such as 2,4-D. Consequently, most incidents involving dicamba exposure also involved exposure to other pesticides as well. There were too few reports of ill effects from exposure to Dicamba in the available data bases to draw conclusions about likely effects. Reigart and Roberts (1999) state that dicamba can be moderately irritating to skin and respiratory tract. This is consistent with reported symptoms from Poison Control Centers.

4.2 Other Pesticide Epidemiology Published Literature

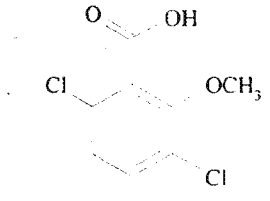
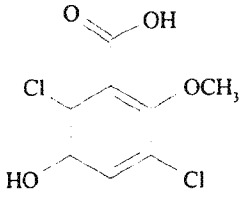
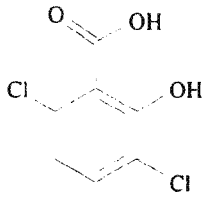
Two epidemiology studies evaluated pesticides and non-Hodgkin's lymphoma (NHL). One study examined residential use and concluded there was "no detectable excess associated with residential exposures" which, for dicamba, were more prevalent in controls than cases. The second study was a multicenter population-based incidence study. In the multivariate model which included exposure to other major pesticides, history of cancer in the case or relatives to the case subject, there was a two-fold risk for dicamba mixtures (odds ratio = 1.96; 95% confidence interval 1.40-2.75) and similar risks were seen for mecoprop and aldrin. The authors concluded that "In our final models, NHL was associated with a personal history of cancer; a history of cancer in first-degree relatives; and exposure to dicamba-containing herbicides, to mecoprop, and to aldrin." The Health Effects Division concludes that this study suggests that dicamba may be associated with NHL, but that the evidence for this association is not strong enough to identify dicamba as a likely or probable cause of NHL. The Agricultural Health Study is planning to assess NHL in the next year; further assessment that will permit a more definitive conclusion concerning dicamba will be available at that time.

5.0 Dietary Exposure/Risk Characterization

5.1 Pesticide Metabolism and Environmental Degradation

5.1.1 Metabolism in Primary Crops

The nature of the residue in plants is adequately understood based on the aggregate of metabolism studies conducted on several crops. The results of these studies indicate that dicamba is rapidly absorbed and translocated by grasses, grapes, black valentine beans, wheat, bluegrass, and soybeans. It is also rapidly absorbed by sugarcane following foliar application but it is very slowly translocated from the leaves to the roots. The metabolism of dicamba in plants proceeds mainly by demethylation and hydroxylation. Major metabolites found include 3,6-dichloro-5-hydroxybenzoic acid (5-OH dicamba) metabolite and 3,6-dichloro-2-hydroxybenzoic acid metabolite, also referred to as 3,6-dichlorosalicylic acid (DCSA). The chemical names and structures of dicamba and its regulated metabolites are depicted below in Table 5.1.

Table 5.1. Chemical names and structures of dicamba and its metabolites.		
		
Dicamba (3,6-dichloro-*o*-anisic acid)	**5-hydroxy dicamba** (3,6-dichloro-5-hydroxy-*o*-anisic acid)	**DCSA** (3,6-dichloro-2-hydroxybenzoic acid or 3,6-dichlorosalicylic acid)

The 8/12/83 Residue Chemistry Chapter of the Dicamba Registration Standard and the 6/30/89 Residue Chemistry Chapter of the Dicamba (SRR) Registration Standard concluded that the major residues found in barley, corn, cotton, grasses, oat, proso millet, sorghum, sugarcane, and wheat are dicamba and its 3,6-dichloro-5-hydroxybenzoic acid (5-OH dicamba) metabolite. It also concluded that in asparagus, the residues of concern are dicamba and DCSA and in aspirated grain fractions and soybeans the residues of concern are dicamba, 5-OH dicamba, and DCSA.

No new data are available or required. HED concludes that these residues are appropriate for the tolerance expression and risk assessment.

5.1.2 Metabolism in Rotational Crops

The nature of the residue in rotational crops is understood. The results of an acceptable confined rotational crop study showed that at a plantback interval of 120 days, the total radioactive residues were <0.01 ppm in/on samples of collard greens (a representative of leafy vegetables) and carrots (a representative of root crops) but were >0.01 ppm in the matrices of barley (a representative of small grains). Residue characterization of barley matrices from the 120-day rotation showed that a relatively high percentage of TRR was associated with natural plant constituents (lignin and cellulose). Therefore, tolerances are not required for rotational crops.

5.1.3 Metabolism in Livestock

The nature of the residue in animals is adequately understood based on acceptable metabolism studies conducted on ruminants and poultry. The compounds identified in these studies include dicamba, 3,6-dichlorosalicylic acid (DCSA) and 2-amino-3,6-dichlorophenol.

In a ruminant metabolism study, dicamba *per se*, accounting for 63.28-92.82% of the TRR, was detected in kidney, liver, and fat. The metabolite DCSA was a major metabolite in kidney (10.55% TRR; 0.0057 ppm) and liver (11.77% TRR; 0.0017 ppm) and only a minor component in fat (1.23% TRR; 0.0001 ppm). An unknown, accounting for <10% of the TRR was detected in liver. A trace (0.006% TRR) of 5-OH dicamba (a plant dicamba metabolite) was detected in urine. Dicamba metabolism in ruminants is proposed by the registrant to proceed via formation of DCSA or 5-OH dicamba.

In a poultry metabolism study conducted at twice the maximum theoretical dietary burden dicamba *per se* accounted for 61.16% and 95.25% of the TRR in liver and eggs, respectively. The metabolite 2-amino-3,6-dichlorophenol (2A36DCP) was detected in liver (35.76% TRR;, 0.001 ppm) but not in eggs. The metabolites DCSA and 5-OH dicamba were not detected in liver or eggs but were detected in excreta and together accounted for <3% of the TRR. Dicamba metabolism in poultry is proposed by the registrant to proceed via formation of DCSA subsequently followed by formation of 2A36DCP.

HED does not anticipate the occurrence of quantifiable residues of dicamba or DCSA in poultry eggs and meat as a result of treating crops which are poultry feed items with use patterns likely to result in the highest residues. Therefore, HED concludes that tolerances are not needed in poultry eggs and meat at this time but may be required if additional uses are registered in the future.

5.1.4 Analytical Methodology

There are adequate plant enforcement methods. The Pesticide Analytical Manual (PAM) Vol. II lists Method I (AM 0268A), a GC method with electron capture detection (GC/ECD) for the enforcement of dicamba plant tolerances. The sensitivity of the method is listed at 0.05 ppm and can determine residues of dicamba, 5-hydroxy-dicamba, and DCSA. For the enforcement of animal commodity tolerances, PAM Vol. II lists Method II, a GC/ECD method which is identical to Method I. The sensitivity of the method is listed at 0.01 ppm. Based on the results of animal metabolism study, which showed that acid hydrolysis can additionally extract up to 30% of TRR in goat liver, HED is requiring the registrants to revise/improve Method II to include an acid hydrolysis step and submit additional validation data. Method II should also be re-written specifically for the analysis of the parent dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid metabolite in animal matrices.

According to FDA's PAM Volume I, Appendix II, dicamba is completely recovered using Section 402 E2 of Protocol B but is only partially recovered using Section 402 E1 of Protocol B. There are no multiresidue methods recovery data for the dicamba metabolites of concern (5-OH dicamba and DCSA), and these data are required.

5.1.5 Environmental Degradation

Aerobic soil metabolism is the main degradative process for dicamba. A single observed half-life for dicamba was six days, with formation of the intermediate non-persistent degradate DCSA. DCSA degraded at roughly the same rate as dicamba; the final metabolites were carbon dioxide and microbial biomass. Dicamba is stable to abiotic hydrolysis at all pH's and photodegrades slowly in water and on soil. Dicamba is more persistent under anaerobic soil:water systems in the laboratory, with a half-life of 141 days. The major degradate under anaerobic conditions was DCSA, which was persistent, comprising > 60% of the applied after 365 days of anaerobic incubation. No other anaerobic degradates were present at > 10% during the incubation. There are no acceptable data for the aerobic aquatic metabolism of dicamba; supplemental information indicates that dicamba degrades more rapidly in aquatic systems when sediment is present.

Dicamba is very soluble in water and very mobile, based on laboratory studies. Because dicamba is not persistent under aerobic conditions, very little dicamba could be expected to leach to

groundwater. If any dicamba did reach anaerobic ground water, it would be somewhat persistent (due to its anaerobic half-life of 141 days); any DCSA that reached ground water would be expected to persist. Results from two acceptable field dissipation studies conducted with dimethylamine salt of dicamba, indicated that dicamba dissipated with a half-life range of 4.4 to 19.8 days. The DCSA was the major degradate in both studies. Both, dicamba and its degradate (DCSA) were found in soil segments deeper than 10 cm.

5.1.6 Comparative Metabolic Profile

Metabolism in rats appears to be less extensive than that observed in the plant and livestock metabolism studies. In the rats study rapid absorption of dicamba was observed, but minimal metabolism was observed as more than 95% of the dosing material was recovered as dicamba. Dicamba metabolism in ruminants is proposed by the registrant to proceed via formation of DCSA or 5-OH dicamba. Dicamba metabolism in poultry is proposed by the registrant to proceed via formation of DCSA subsequently followed by formation of 2A36DCP. DCSA and 5-OH-dicamba were major plant metabolites, and DCSA was the only significant environmental degradate that could potentially be found in drinking water.

5.1.7 Pesticide Metabolites and Degradates of Concern

A summary of dicamba metabolites and environmental degradates to be included in the dietary risk assessment and tolerance expression may be found in Table 5.2. DCSA and 5-OH- dicamba are major metabolites, and in the case of DCSA, a major degradate that could potentially be found in drinking water. Specific toxicity data are not available for either of these compounds. Based on their structural similarity to the parent, the risk assessment team has concluded that they may have similar toxicity as the parent, and should be included in the dietary risk assessment.

Table 5.2 Summary of Dicamba Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression [1]

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop - Most grains	Dicamba and 5-OH Dicamba	Dicamba and 5-OH Dicamba
	Primary Crop - Asparagus	Dicamba and DCSA	Dicamba and DCSA
	Primary Crop - Soybean and Aspirated Grain Fractions	Dicamba, DCSA, and 5-OH Dicamba	Dicamba, DCSA, and 5-OH Dicamba
	Rotational Crop	Not Required [2]	Not Required [2]
Livestock	Ruminant	Dicamba and DCSA	Dicamba and DCSA
	Poultry	Not Required	Not Required

Table 5.2	**Summary of Dicamba Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression** [1]	
Matrix	Residues included in Risk Assessment	Residues included in Tolerance Expression
Drinking Water	Dicamba and DCSA	Not Applicable

[1] Nomenclature of metabolites/degradates: 3,5-dichloro-5-hydroxybenzoic acid = 5-OH; 3,6-dichloro-2-hydroxybenzoic acid = 3,6-dichlorosalicylic acid = DCSA;
[2] Tolerances and dietary risk assessment are not required provided the registrants specify a 120-day plant-back interval.

5.1.8 Drinking Water Residue Profile

5.1.8.1 Surface Water

PRZM-EXAMS simulations were conducted for Dicamba acid and its degradate DCSA use on sugarcane to evaluate the cumulative probability distribution for peak and annual mean Estimated Drinking Water Concentrations (EDWCs). A summary of the EDWCs may be found in Table 5.3.

Table 5.3. Estimated Drinking Water Concentrations to Be Used for Exposure to Dicamba Acid, and its Degradate Dichlorosalicylic Acid (DCSA) in Drinking Water						
Crop	Model EDWCs (µg/L)					
	Dicamba			DCSA		
	Acute	One-in-10-year annual mean	36 year overall mean	Acute	One-in-10-year annual mean	36 year overall mean
Surface Water						
FL-Sugarcane (Ground)	357	13	5.23	10.1	0.75	0.4
FL-Sugarcane (Aerial)	346	12.9	5.38	10.9	0.813	0.47
LA-Sugarcane (Ground)	233	9.74	3.13	8.79	0.66	0.32
LA-Sugarcane (Aerial)	230	9.74	3.44	9.74	0.73	0.39
Note that these estimates assume one application @ 2.8 lb ai/A (parent); and 0.446 lb ai/A (DCSA) and a crop area factor of 0.87.						

5.1.8.2 Ground Water

SCIGROW (Screening Concentration in Ground Water) provides a groundwater screening exposure value to be used in determining the potential risk to human health from drinking water contaminated with the pesticide. Since the SCIGROW concentrations are likely to be approached in only a very small percentage of drinking water sources, i.e., highly vulnerable aquifers, it is not appropriate to use SCIGROW for national or regional exposure estimates.

SCIGROW estimates likely groundwater concentrations if the pesticide is used at the maximum allowable rate in areas where groundwater is exceptionally vulnerable to contamination. In most cases, a large majority of the use area will have groundwater that is less vulnerable to contamination than the areas used to derive the SCIGROW estimate. The EDWC for dicamba is 0.016 µg/L and for DCSA is 0.008 µg/L.

Monitoring data are available in the Pesticides in Ground Water Database [Hoheisel et al. 1991] for dicamba (3,172 wells sampled) and 5-hydroxy dicamba (87 wells sampled). Out of the wells sampled, there were no reports of residues greater than the stated MCL (200 µg/L lifetime). Detections were ranging from traces to 44 ppb. The highest detection was for water samples in IN. However, the detection limits are unknown, and it is not known if wells were sampled in areas where dicamba was used. The US Geological Survey National Water Quality Assessment program (NAWQA) has analyzed for dicamba in their samples for surface and groundwater. A total of 6614 surface water samples were collected between 1993 and 2003 with 201 detections ranging from 0.009 to 1.76 ppb. The highest detection was for water samples in FL. A total of 6571 ground water samples were collected between 1993 and 2004, with 149 detections ranging from 0.008 to 2.50 ppb. The highest detection was for water samples in GA. The major degradate for dicamba, DCSA was not analyzed for by the NAWQA.

The highest value found in the Pesticides in Ground Water Database is higher than the modeled value. Therefore, a scoping assessment using the highest monitoring value was conducted.

5.1.9 Food Residue Profile

Tolerance-level residues and 100% crop treated were assumed for all crops in this assessment. If sufficient data were available to reassess tolerances, then the reassessed values were used. The established values were used for most commodities with the exception of the livestock commodities and sorghum. All processing factors were assumed to be 1, though the available processing data suggest that residue concentrations are reduced upon processing. The tolerance reassessment summary may found in Appendix C of this document.

5.1.10 International Residue Limits

No Codex MRLs have been established for dicamba; therefore, issues of compatibility between Codex MRLs and U.S. tolerances do not exist. Compatibility cannot be achieved with the Canadian negligible residue limits or with Mexican MRLs because these levels are expressed in terms of parent compound only.

5.2 Dietary Exposure and Risk

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 2.03), which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analyses were performed to support the reregistration eligibility decision - Phase I. Results of the analyses for food alone may be found in Table 5.4 and for food and drinking water from surface water sources may be found in Table 5.5. The latter table also includes a scoping assessment for chronic dietary exposures using the highest value found in the Pesticides in Ground Water database.

Table 5.4. Summary of Dietary Exposure and Risk for Dicamba - Food Only

Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.0297	3.0	0.0115	2.6
All Infants (< 1 year old)	0.0516	5.2	0.0189	4.2
Children 1-2 years old	**0.0536**	**5.4**	**0.0292**	**6.5**
Children 3-5 years old	0.0483	4.8	0.0266	5.9
Children 6-12 years old	0.0354	3.5	0.0182	4.1
Youth 13-19 years old	0.0233	2.3	0.0111	2.5
Adults 20-49 years old	0.0214	2.1	0.00946	2.1
Adults 50+ years old	0.0150	1.5	0.00721	1.6
Females 13-49 years old	0.0180	2.9	0.00843	1.9

*The population subgroup that has the most exposure is bolded.

Table 5.5. Summary of Dietary Exposure and Risk for Dicamba - Food and Water

Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary - Surface Water		Chronic Dietary - Ground Water	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.0435	4.4	0.0118	2.6	0.0124	2.7
All Infants (< 1 year old)	**0.108**	**11**	0.0199	4.4	0.0217	4.8
Children 1-2 years old	0.0756	7.6	**0.0297**	**6.6**	**0.030**	**6.8**
Children 3-5 years old	0.0675	6.8	0.0270	6.0	0.0278	6.2

Table 5.5. Summary of Dietary Exposure and Risk for Dicamba - Food and Water						
Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary - Surface Water		Chronic Dietary - Ground Water	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*	Dietary Exposure (mg/kg/day)	% cPAD*
Children 6-12 years old	0.0476	4.8	0.0185	4.1	0.019	4.2
Youth 13-19 years old	0.0318	3.2	0.0113	2.5	0.0117	2.6
Adults 20-49 years old	0.0341	3.4	0.00973	2.2	0.0102	2.3
Adults 50+ years old	0.0267	2.7	0.00750	1.7	0.00804	1.8
Females 13-49 years old	0.0312	3.1	0.00870	1.9	0.00922	2.0

*The population subgroup that has the most exposure is bolded.

Estimated exposure to dicamba and its residues of concern for all population sub-groups are all well below the level of concern. The most highly exposed subgroup for both acute and chronic exposure is children, aged 1-2. Acute exposures are at 5.4 and 7.6% of the acute Population Adjusted Dose (aPAD) for food and food plus water, respectively. Chronic exposures are at 6.5, 6.6 and 6.8% of the chronic Population Adjusted Dose (cPAD) for food, food plus drinking water (from surface water sources), and food plus drinking water (from ground water sources) respectively. When considering acute exposure in food and water combined, the most highly exposed subgroup is infants with 11% of the aPAD consumed.

Actual exposure is likely to be considerably lower. These assessments assume all commodities have tolerance level residues, but residues in most field trials are lower. The assessments also assume all crops are treated, but a screening level usage analysis (M. Kaul, 9/20/04) indicate that the percent crop treated for most commodities is less than 20 %. Only drinking water from surface water sources were considered, but the model estimates for ground water are much lower than surface water estimates.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

According to the EPA Pesticide Sales and Usage Report for 2000/2001, dicamba is ranked number seven among the ten most commonly used conventional pesticide active ingredients in the home and garden market sector.

The residential products are typically formulated as dry weed and feed products or as liquids in concentrates or ready to use sprays. Many of these formulations include other herbicides such as 2,4-D and MCPP-p. Both spot and broadcast treatments are included on the labels. Exposures are expected to be short term in duration for broadcast treatments because the label allows only two broadcast treatments per year. Exposures are also expected to be short term in duration for

spot treatments because the labels recommend repeat applications in two to three weeks for hard to kill weeds.

6.1 Residential Handler Exposure and Risk Estimates

6.1.1 Residential Handler Exposure Assessment

Scenarios

The following scenarios were assessed:

1. Hand Application of Granules
2. Belly Grinder Application
3. Load/Apply Granules with a Broadcast Spreader
4. Mix/Load/Apply with a Hose-end Sprayer (Mix your own)
5. Mix/Load/Apply with a Hose-end Sprayer (Ready to Use)
6. Mix/Load/Apply with Hand Held Pump Sprayer
7. Mix/Load/Apply with Ready to Use Sprayer

Data Sources

The handler exposure data were taken from the Pesticide Handler Exposure Database (PHED) and the Outdoor Residential Exposure Task Force (ORETF). Exposure data for scenarios #1 and #2 were taken from PHED. Exposure data for scenarios #3, #4 and #5 were taken from the residential portion of the ORETF Handler Study. Exposure data for scenarios #6 and #7 were taken from MRID 444598-01, which has recently been purchased by the ORETF. This study involved low pressure handwand and RTU trigger sprayer application of carbaryl to home vegetable plants.

Assumptions Regarding Residential Applicators

- Clothing would consist of a short-sleeved shirt, short pants and no gloves.
- Broadcast spreaders and hose end sprayers would be used for broadcast treatments and the other application methods would be used for spot treatments only.
- An area of 0.023 acre (1000 square feet) would be treated per application during spot treatments and an area of 0.5 acre would be treated during broadcast applications.
- The application rate is 1.0 lb ae/acre as listed in the Dicamba Use Closure Memo.

6.1.2 Residential Handler Risk Estimates

A summary of the margin of exposure (MOE) estimates is included in Table 6.1. All of the MOEs exceed the target MOE of 100 and the risks are not of concern. The residential handler risks were calculated using standard assumptions, the highest quality unit exposure data available, and the maximum label application rates.

Table 6.1 Dicamba Short Term MOEs for Homeowner Applications to Lawns (Application Rate = 1.0 lb ai/acre)			
Scenario	**Treated Area (acres/day)**	**Combined Dose (mg/kg/day)**	**Combined MOE[A]**
1 Hand Application of Granules	0.023	0.0058	7800
2 Belly Grinder Application	0.023	0.0054	8300
3. Load/Apply Granules with a Broadcast Spreader	0.5	0.00073	62000
4. Mix/Load/Apply with a Hose-end Sprayer (Mix your own)	0.5	0.012	3800
5. Mix/Load/Apply with a Hose-end Sprayer (Ready to Use)	0.5	0.0029	16000
6. Mix/Load/Apply with Hand Held Pump Sprayer	0.023	0.0019	24000
7. Mix/Load/Apply with Ready to Use Sprayer	0.023	0.0027	17000
A. The target MOE is 100.			

6.2. Residential Postapplication Exposure and Risk Estimates

6.2.1 Residential Postapplication Exposure Assessment

Scenarios

The following exposure scenarios are assessed for residential post application risks

- Acute and Short Term Exposures of Toddlers Playing on Treated Turf
- Acute and Short Term Exposures of Adults Performing Yardwork on Treated Turf
- Acute and Short Term Exposures of Adults Playing Golf on Treated Turf
- Acute Exposures of Toddlers from Incidental Oral Ingestion of Granules

Data Sources

There are three turf transferable residue studies (MRID 446557-02, 450331-01 and 446557-03 that were submitted by the Broadleaf Turf Herbicide TFR Task Force. The field portion of the studies were conducted by Grayson Research LLC of Creedmoor, North Carolina, AGSTAT of Verona, Wisconsin, and Research for Hire of Porterville, California. The laboratory analysis for all three studies was conducted by Covance Laboratories of Madison, Wisconsin. These studies measured the dissipation of several phenoxy herbicides, including Dicamba, using the ORETF roller technique (which is also called the modified California Roller).

There was an additional study (MRID 449590-01) that was submitted by Novartis Crop Protection. The field portion of this study was conducted by Research Options, Inc of Winter Garden, Florida, ABC Laboratories California of Madera, California and Crop Management Strategies of Germansville, PA. The laboratory analysis for all three sites was conducted by ABC Laboratories of Columbia, Missouri. This study also used the ORETF roller technique.

All of the studies were reviewed by HED and were found to meet all of the series 875 guidelines for postapplication exposure monitoring.

Application of the TTR Data

A summary of the data used for exposure assessment is included in Table 9.2

Table 6.2 - Summary of TTR Data Used for Post Application Exposure Assessment		
MRID	**449590-01**	**450331-01**
Location	Florida	California
Precipitation	No Rain	No Rain
Application Rate (lb ae/acre)	1.0	0.21
Maximum TTR (ug/cm^2)	0.29	0.033
Maximum TTR (percent of application rate)	2.6 - Note 1	1.3
Day 0 Average TTR (ug/cm^2)	0.10	0.033
Day 0 Average TTR (percent of application rate)	0.90	1.3 - Note 2
Semi-log Slope Factor	N/A	-0.38 - Note 2
7 day Average TTR (ug/cm^2)	N/A	0.013
7 day Average TTR (percent of application rate)	N/A	0.55 - Note 2
Note 1 - This value was used to derive the TTR for 1day acute exposures. Note 2 - These values were used to derived the TTR for seven day average short term exposures.		

General Assumptions

The following general assumptions are taken from the Standard Operating Procedure (SOPs) of December 18. 1997 and ExpoSAC Policy #12 "Recommended Revisions to the Standard Operating Procedures for Residential Exposure Assessments of February 22, 2001.

- The TTR values were used for calculating dermal exposures on turf because they were greater than 1.0% of the application rate. These values were adjusted for application rates as needed
- An assumed initial TTR value of 5.0% of the application rate is used for assessing hand to mouth exposures.
- An assumed initial TTR value of 20% of the application is used for assessing object to mouth exposures.
- Soil residues are contained in the top centimeter and soil density is 0.67 mL/gram.
- Three year old toddlers are expected to weigh 15 kg.
- Hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm^2 representing the palmar surfaces of three fingers.
- Saliva extraction efficiency is 50 percent meaning that every time the hand goes in the mouth approximately ½ of the residues on the hand are removed.

- Adults are assessed using a transfer coefficient of 14,500 cm^2/hour.
- Toddlers are assessed using a transfer coefficient of 5200 cm^2/hour.
- Golfers are assessed using a transfer coefficient of 500 cm^2/hour.
- An exposure duration of 2 hours per day is assumed for toddlers playing on turf or adults performing heavy yardwork.
- An exposure duration of 4 hours is assumed for playing golf.
- The assumed ingestion rate is 0.3 gram/day. This is based on the assumption that if 150 lbs of product were applied to a ½ acre lawn, the amount of product per square foot would be 3 g/ft^2 and a child would consume one-tenth of the product available in a square foot.
- The percent ai in granular formulations used in residential settings was assumed to be in the range of 0.1 to 1.0 percent based upon the product labels listed in OPPIN.

Assumptions Specific to Dicamba

The following assumptions that are specific to Dicamba are used for assessing residential post application exposures.

- The application rate of 1.0 lbs ae/acre as stated in the Use Closure Memo was used.

Calculation Methods

The above factors were used in the standard SOP formulas to calculate the exposures. MOEs were calculated for acute dermal and incidental oral exposures using the maximum TTR value along with the acute dietary LOAEL of 300 mg/kg/day for children and NOAEL of 62.5 mg/kg/day for females, aged 13-49. MOEs for short term exposures were calculated using the seven day average TTR value, because the short term dermal NOAEL of 45 mg/kg/day was based upon decreased pup body weight gain which did not occur until after several days of exposure.

6.2.2 Residential Postapplication Risk Estimates

The MOEs for acute exposures are summarized in Table 6.3. All of the acute MOEs for both adult and toddler exposures exceed the respective target MOEs of 100 and 300, so the risks for adults and toddler exposures are not of concern.

Table 6.3 - Acute Dicamba MOEs for Turf Exposures (Application Rate = 1.0 lb ae/acre)							
Scenario	**TTR (ug/cm^2)**	**TC (cm^2/hr)**	**Dermal MOE**	**Hand-to Mouth MOE**	**Object to Mouth MOE**	**Soil Ingestion MOE**	**Total MOE[B]**
Toddlers (BW = 15 kg)							
Playing	0.29[A]	5,200	9,900	20,000	80,000	5,900,000	6,100
Adults (BW = 70 kg)							
Yardwork Golfing	0.29[A]	14,500 500	17,000 240,000	N/A			

A. This value was derived from the maximum TTR of 2.6 percent from MRID 449590-01.
B. Total MOE = 1/((1/Dermal MOE) + (1/Hand-to-Mouth MOE)+ (1/Object-to-Mouth MOE)+(1/Soil Ingestion MOE)).

The target MOE is 300 for adult and toddler exposures.

The MOEs for short term exposures are summarized in Table 6.4. All of the short term MOEs for both adult and toddler exposures exceed the target MOE of 100.

Table 6.4. Short Term Dicamba MOEs for Turf Exposures (Application Rate = 1.0 lb ae/acre)							
Scenario	**TTR (ug/cm^2)**	**TC (cm^2/hr)**	**Dermal MOE**	**Hand-to Mouth MOE**	**Object to Mouth MOE**	**Soil Ingestion MOE**	**Total MOE[B]**
Toddler Exposures (BW = 15 kg)							
Playing	0.060[A]	5200	7,200	7,200	29,000	2,100,000	3,200
Adult Exposures (BW = 70 kg)							
Yardwork	0.060[A]	14500	12,000	N/A			
Golfing	0.060[A]	500	170,000				

A. Seven day average TTR derived from the California TTR Study MRID 450331-01.
B. Total MOE = 1/((1/Dermal MOE) + (1/Hand-to-Mouth MOE)+ (1/Object-to-Mouth MOE)+(1/Soil Ingestion MOE))

The target MOE for adult and toddler exposures is 100.

The acute margins of exposures from toddlers ingesting granules are summarized in Table 6.5. All of the MOEs exceed 300, and are not of concern.

Table 6.5 Granule Ingestion Risks for Dicamba

Percent ai	Potential Dose Rate[1] (mg/day)	Absorbed Dose[2] (mg/kg/day)	Acute MOE[3]
0.1	0.3	0.02	15000
0.5	1.5	0.1	3000
1.0	3.0	0.2	1500

1. Potential Dose Rate (PDR) = 0.3 gram/day * Percent ai* 1000 mg/gram
2. Absorbed Dose = PDR/BW
3. MOE = NOAEL/Dose where the NOAEL = 300 mg/kg/day

The calculation of acute MOEs using a maximum TTR value for toddler turf post application exposure represents a policy change, because the maximum TTR values were previously only used to calculate short term MOEs. The dicamba risk assessment team decided that the previous approach would greatly overestimate the short term risks, because the short term incidental oral and dermal endpoints were based upon effects that would only occur after several days of exposure. The team also decided that the single day exposures as represented by the maximum TTR values would be more appropriately assessed using the acute dietary endpoints. The short term exposures were assessed using the seven day average TTR values because the endpoints occurred after several days of exposure and because the TTR data were collected during a seven day time period.

The actual use rates of dicamba are typically less than the maximum label rates because dicamba is usually mixed with other herbicides such as 2,4-D and MCPP-p.

6.3 Other (Spray Drift, etc.)

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for the dicamba. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. On a chemical by chemical basis, the Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift with specific products with significant risks associated with drift.

7.0 Aggregate Risk Assessments and Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure.

7.1 Acute Aggregate Risk

Acute, or less than one day, exposures may result from consuming treated food, drinking water, or residential exposures such as yard work for adults, playing golf on treated turf, or playing in treated turf for children. Typically HED does not aggregate acute food exposures with acute residential exposures. The acute food exposure estimates consider higher food consumption with maximum residue values and the estimated drinking water estimates are high-end values as well. It is very unlikely that high end food and water exposures will occur on the same day as the maximum residential exposures.

The aggregate food and water assessment results are presented in Table 7.1. The most highly exposed subgroup is infants (<1 year old) at 11% of the aPAD, which is well below the level of concern. As stated previously, actual exposures are likely to be much lower because the food assessment assumes 100% crop treated and tolerance level residues.

Table 7.1. Aggregate Acute Assessment for Dicamba - Food and Water

Population Subgroup*	Acute Dietary (95th Percentile)	
	Dietary Exposure (mg/kg/day)	% aPAD
General U.S. Population	0.0435	4.4
All Infants (< 1 year old)	**0.108**	**11**
Children 1-2 years old	0.0756	7.6
Children 3-5 years old	0.0675	6.8
Children 6-12 years old	0.0476	4.8
Youth 13-19 years old	0.0318	3.2
Adults 20-49 years old	0.0341	3.4
Adults 50+ years old	0.0267	2.7
Females 13-49 years old	0.0312	5.0
Drinking water exposures are from surface water sources.		

7.2 Short-Term Aggregate Risk

The short term aggregate assessment considered exposures from food, water, residential handles, and residential post-application activities. Average food and water exposure estimates were used in the assessment. The residential handler scenario that resulted in the highest exposures, mix/load/apply with a (mix your own) hose-end sprayer, was used in the handler assessment. The exposures from the yardwork post-application scenario was used for the adult assessment, and the exposures from the toddler playing in turf scenario was used in the child assessment. The other scenario considered was the same adult applying dicamba with the hose-end sprayer and then doing yardwork in the treated area.

The results of all of the short-term aggregate assessments are presented in Table 7.2. HED is generally not concerned if the margins of exposure (MOEs) exceed the target, which for this assessment is 100. The MOEs for all scenarios are greater than 100 so are not of concern. As stated in the previous section, these are likely to be overestimates and the actual exposures are probably much lower.

Table 7.2. Short-Term Aggregate Risk Calculations For Dicamba

Population	Food + Water Exposure mg/kg/day	Incidental Oral Exposure, mg/day	Dermal Dose, mg/kg/day	Combined Exposure, mg/kg/day	MOE Food + Water+ Incidental Oral + Dermal
Adult Male - Handler	0.012822	0	0.0102	0.023	1950
Adult Male - Post - App	0.012822	0	0.0037	0.01652	2720
Child - Post - App	0.029662	0.0078	0.0062	0.04366	1030

Note: HED is generally not concerned if the MOE exceeds the target of 100.
The adult handler assessment is from the scenario that had the highest exposure, Mix/Load/Apply with a Hose-end Sprayer (Mix your own). The adult post-application assessment is from the yard work scenario. The exposures for the child post-application scenario are from a toddler playing on treated turf. Average food and water exposures were used in this assessment. Adult Male food consumption was used for the food and water values because they have greater exposure.

7.3 Intermediate-Term Aggregate Risk

There are no residential scenarios that would result in intermediate-term (1 month to 6 month) residential exposures. Additionally, the same toxicity study was used as the endpoint for all short-, intermediate-, and long-term assessments, so the short-term assessment is protective of all of these exposures. An intermediate-term assessment is not required.

7.4 Long-Term Aggregate Risk

There are no residential scenarios that would result in long term (greater than six month)

exposures, so only food and water need be aggregated for this assessment. Results of the chronic assessment are presented in Table 7.3.

The most highly exposed subgroup is children, aged 1-2 years old, at 6.6% of the cPAD. Again, this is an exaggerated assessment as it assumes 100 percent crop treated and tolerance-level residues. Actual exposure is likely to be much lower.

Table 7.3. Summary of Dietary Exposure and Risk for Dicamba - Food and Water

Population Subgroup*	Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.0118	2.6
All Infants (< 1 year old)	0.0199	4.4
Children 1-2 years old	**0.0297**	**6.6**
Children 3-5 years old	0.0270	6.0
Children 6-12 years old	0.0185	4.1
Youth 13-19 years old	0.0113	2.5
Adults 20-49 years old	0.00973	2.2
Adults 50+ years old	0.00750	1.7
Females 13-49 years old	0.00870	1.9

7.5 Cancer Risk

In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), dicamba is classified as "Not Likely to be Carcinogenic to Humans". This was based on negative cancer studies in rats and mice which were tested at adequate dose levels to assess the carcinogenicity of dicamba Therefore, this risk assessment is not required.

8.0 Cumulative Risk Characterization/Assessment

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to dicamba and any other substances, and dicamba does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that dicamba has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on

EPA's website at http://www.epa.gov/pesticides/cumulative/.

9.0 Occupational Exposure/Risk Pathway

9.1 Short/Intermediate Handler Risk

9.1.1 Exposure

9.1.1.1 Exposure Scenarios

Based upon the application methods for occupational uses of dicamba, the following exposure scenarios were assessed.

Mix/Load Wettable Powder
Mix/Load Water Dispersible Granules
Mix/Load Liquid Formulations
Load Granules
Aerial Application
Groundboom Application
Turfgun Application
Backpack application
Right of Way Application
Broadcast Spreader Application
Mix/Load/Apply Liquids with a Backpack Sprayer
Mix/Load/Apply Wettable Powder with a Turfgun
Mix/Load/Apply Wettable Powder with a Water Dispersible Granules
Mix/Load/Apply Liquids with a Turfgun
Load/Apply Granules with a Push Cyclone
Flag Aerial Application

9.1.1.2 Occupational Handler Exposure Assumptions and Data Sources

Exposure Assumptions

The following assumptions and factors were used in order to complete the exposure and risk assessments for occupational handlers/applicators:

- The average work day was 8 hours.
- The daily acreages treated were taken from EPA Science Advisory Council for Exposure Standard Operating Procedure #9 "Standard Values for Daily Acres Treated in Agriculture," Revised July 5, 2000. These values are listed in Table 6.
- The application rates are the maximum rates as listed in the Dicamba Use Closure Memo.
- A body weight of 70 kg was assumed because the endpoint is not gender specific.
- The inhalation absorption rate is 100%.
- Baseline PPE includes long sleeve shirts, long pants and no gloves or respirator.
- Single Layer PPE includes baseline PPE with chemical resistant gloves.
- Double Layer PPE includes coveralls over single layer PPE.
- PF5 indicates a filtering facepiece respirator (i.e. a dustmask) with a protection factor of 5 when properly fitted.

- PF10 indicates a half mask elastomeric facepiece respirator with a protection factor of 10 when properly fitted and used with appropriate cartridges.
- Only closed cockpit airplanes are used for aerial application.
- Airplane pilots do not wear chemical resistant gloves.

Handler Exposure Data Sources

The handler exposure data were taken from the Pesticide Handler Exposure Database (PHED), the Outdoor Residential Exposure Task Force (ORETF) and the California Department of Pesticide Regulation (CA DPR). The PHED data were used primarily for the large scale agricultural and forestry scenarios and the ORETF data were used for lawn care scenarios. The CA DPR data were used for the backpack applicator forest site preparation scenario where multiple applicators are supplied by a nurse tank.

9.1.2 Occupational Handler Risk Estimates and Characterization

A summary of the risk estimates for occupational handlers is presented in Table 9.1. The margins of exposure for some of the baseline exposure scenarios are below the target of 100. However, if a single layer of protection or engineering controls are added to these scenarios, then all of the occupational exposure estimates have margins of exposure exceeding 100, so none of are of risk concern.

The actual use rates of dicamba are typically less than the maximum label rates because dicamba is usually mixed with other herbicides such as 2,4-D to increase the spectrum of weeds controlled.

Only a few dicamba products are formulated as wettable powders and most of these products are packaged in water soluble bags that are used on turf.

Many of the labels require waterproof gloves instead of chemical resistant gloves. It is not known if these gloves provide adequate protection.

Table 9.1 Dicamba Handler Combined MOEs

Exposure Scenario	Crop or Site	Application Rate (lb ae/acre)	Acres/ Day	Margins of Exposure		
				Base-line	Single Layer	Engineering Control
Mixer/Loader (M/L)						
M/L WP for Groundboom	Golf Courses	1	40	130	>1000	>1000
M/L WP for Turfgun Application	turf	1	5	>1000	>1000	>1000
M/L WDG for Aerial	Fallow Land	2	1200	120	120	NA
M/L WDG for Aerial	Corn	0.5	1200	490	490	NA
M/L WDG for Groundboom	Fallow Land	2	200	740	740	NA
M/L WDG for Groundboom	Corn	0.5	200	>1000	>1000	NA
M/L WDG for Groundboom	Golf Courses	1	40	>1000	>1000	NA
M/L WDG for Turf Gun	Turf	1	100	>1000	>1000	NA

Table 9.1 Dicamba Handler Combined MOEs

Exposure Scenario	Crop or Site	Application Rate (lb ae/acre)	Acres/ Day	Margins of Exposure		
				Base-line	Single Layer	Engineering Control
M/L Liquids for Aerial	Sugar Cane	2.8	1200	**2**	200	**680**
M/L Liquids for Aerial	Soybeans, RPF	2	1200	**3**	280	**960**
M/L Liquids for Aerial	Small Grains, Corn	0.5	1200	**12**	>1000	>1000
M/L Liquids for Groundboom	Sugar Cane	2.8	200	**13**	>1000	>1000
M/L Liquids for Groundboom	Soybean, RPF	2	200	**18**	>1000	>1000
M/L Liquids for Groundboom	Small Grains, Corn	0.5	200	**72**	>1000	>1000
M/L Liquids for Groundboom	Sod Farms	1	80	**90**	>1000	>1000
M/L Liquids for Groundboom	Golf Courses	1	40	**180**	>1000	>1000
M/L Liquids for ROW Sprayer	Right of Way Areas	2	50	**72**	>1000	>1000
M/L Liquids for Turf Gun	Turf	1	100	**72**	>1000	>1000
M/L Liquids for Backpack Application	Forest Site Prep	2	40	**90**	>1000	>1000
Load Granulars for Broadcast Spreader	Golf Courses	1.5	40	>1000	>1000	>1000
Applicator (APP)						
Aerial Application	All crops above	0.5 to 2.8	1200	ND	ND	>1000
Groundboom Application	All crops above	0.5 to 2.8	40 to 200	>1000	>1000	>1000
ROW Application	ROW	2	50	160	500	ND
Back Pack Application	Forest Site Prep	1.0	4	ND	410	ND
Turfgun Application	Turf	1.5	5	ND	>1000	ND
Broadcast Spreader Application	Golf Courses	1.5	40	>1100	>1000	>1000
Mixer/Loader/Applicator (M/L/A)						
M/L/A Wettable Powder with Turfgun	turf	1	5	ND	>1000	>1000
M/L/A WDG with Turfgun	turf	1	5	ND	>1000	ND
M/L/A Liquid Flowables with Turfgun	turf	1	5	ND	>1000	ND
M/L/A Liquids with Backpack Sprayer	ROW, RPF	2	4	ND	970	ND
Load/Apply Granules with a Push Cyclone	turf	1	5	ND	>1000	ND
Flagger						
Flag Aerial Application	All crops above	0.5 to 2.8	1200	>470	>440	>1000

Notes:
Risk estimates are the combined dermal and inhalation exposures.

RPF = Rangeland, Pastures and Fallow Land
ROW = Rights of Way
ND = No Data Available

MOEs that are less than 100 indicate risks of concern and are highlighted in bold font.

9.2 Short/Intermediate/Long-Term Postapplication Risk

Post application Dicamba exposures can occur in the agricultural environment when workers enter fields recently treated with Dicamba to conduct tasks such as scouting and irrigation.

9.2.1 Occupational Post Application Exposure

9.2.1.1 Occupational Post Application Exposure Scenarios

Broadcast applications can be made to grass crops, such as cereal grains, which are tolerant of

dicamba. Because dicamba is typically applied once per season and the relevant agricultural scenarios occur for only a few weeks per year, it is anticipated that dicamba exposures would be primarily short term and, more rarely, intermediate term.

Potential inhalation exposures are not anticipated for the post-application worker scenarios because of the low vapor pressure of dicamba (3.4×10^{-5} mm at 25 C), and the Agency currently has no policy/method for evaluating non-dietary ingestion by workers due to poor hygiene practices or smoking. As a result, only dermal exposures were evaluated in the post-application worker assessment.

9.2.1.2 - Exposure Data Sources and Assumptions

There are three turf transferable residue (TTR) studies that were submitted by the Broadleaf Turf Herbicide TFR Task Force. A summary of the turf transfer coefficients along with characterization of the post-application scenarios as low, medium, or high exposures may be found in Table 9.2

The following assumptions were made regarding occupational post application:

- Risks were assessed using the maximum rates from the Dicamba Use Closure Memo.
- The transfer coefficients are from an interim transfer coefficient policy developed by HED's Science Advisory Council for Exposure using proprietary data from the Agricultural Re-entry Task Force (ARTF) database (US EPA, August 7, 2001). This policy will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.
- The transfer coefficients for turf harvesting and maintenance are based upon recently conducted ARTF studies that are being reviewed by HED.
- The initial percent of application rate as Dislodgeable Foliar Residue (DFR) was assumed to be 20% for all crops except turf. These are the standard values used in the absence of chemical specific data.
- The Maximum TTR value (2.6 percent of the application rate) from the DMA Treatment at the Florida site in the Vanquish Study was used to assess risks of working on turf.

Table 9.2 Post Application Exposure Scenarios and Transfer Coefficients for Dicamba

Crop	Label Directions Post Application Exposure Scenarios	Transfer Coefficient (cm^2/hr)
Asparagus	Apply immediately after cutting. If spray contacts emerged spears, crooking may result. Pre Harvest Interval (PHI) = 24 hours	None[1,2]
Small Grains Barley, Oats, proso millet, triticale, wheat	Apply to fall seeded barley prior to the jointing stage. Apply to spring seed barley before it exceeds the 4 leaf stage. Apply to fall seeded oats prior to the jointing stage. Apply to spring seeded oats before the 5 leaf stage is exceeded. Apply to proso millet at the 2 to 5 leaf stage. Apply to fall seeded triticale or wheat prior to the jointing stage. Apply to spring seeded triticale or wheat before the 6 leaf stage. Low Exposure Scenarios - Irrigation, scouting, immature plants Medium Exposure Scenarios - Same as above on mature plants	 100 1500
Corn	Early Post Emergence - Apply from corn emergence through 5 leaf stage or 8 inches tall, whichever comes first. Late Post Emergence - Apply from 8 to 36 inch corn or to 15 days before tassel emergence, whichever comes first. Low Exposure Scenarios - Scouting, weeding immature plants Medium Exposure Scenarios - Scouting, weeding more mature plants High Exposure Scenarios - Scouting, weeding, irrigation mature plants Very High Exposure Scenarios - Detasseling	 100 400 NA NA
Cotton	N/A - Applied as a preplant treatment.	NA
Pasture, Rangeland, Grassland	PHI = 7 days	None[1]
Sorghum	Post Emergence - Apply when sorghum is in the 3 to 5 leaf stage, but before it is 15" tall. If sorghum is taller than 8" use drop nozzles and keep spray off the foliage. Pre-harvest application (TX and OK only) - apply anytime after soft dough stage (PHI = 30 days) Low Exposure Scenarios - Scouting immature plants High Exposure Scenarios - Irrigation and scouting mature plants	 100 1000
Soybeans	Apply after pods have reached mature brown color and at least 75% leaf drop has occurred (PHI = 14 days)	None[1]
Sugarcane	Apply before canes appear for control of emerged weeds. Apply after canes emerge and through canopy closure. When possible direct sprays beneath the canopy to minimize the likelihood of crop damage. Medium Exposure Scenarios - scouting immature plants High Exposure Scenarios - scouting mature plants	 1000 2000
Turf, Sod Farm and Golf Course	Treat when weeds are young and actively growing. Do not apply more than 1.0 lb per season. Low Exposure Scenarios - Mowing High Exposure Scenarios - Transplanting, hand weeding	 3400 6800

1. Post application exposures are expected to be minimal due to application timing or method.
2. Asparagus plants do not have foliage (i.e. ferns) when the spears are harvested.

9.2.2 Occupational Post Application Risk Estimates

A summary of the worker risks for short/intermediate term post application exposures is given in Table 9.3. All of the short/intermediate term MOEs are above 100 on Day 0 which indicates that

the risks are not of concern. The Worker Protection Standard (WPS) Restricted Entry Interval (REI) for dicamba is 24 hours for the amine and sodium salt forms.

Table 9.3 - Dicamba Postapplication Worker Risks

Crop	Transfer Coefficient Group	Application Rate (lb ae/acre)	Short/Intermediate Term MOE on Day 0		
			Low Exposure Scenarios*	Medium Exposure Scenarios*	High Exposure Scenarios*
Small Grains (i.e. wheat)	Field/row crop, low/medium	0.50	23000	1600	NA
Corn (Early Post Emergence)	Field/row crop, low/medium	0.50	23000	N/A	NA
Corn (Late Post Emergence)	Field/row crop, low/medium	0.25	N/A	12000	N/A
Sorghum	Field/row crop, low/medium	0.25	47000	12000	4700
Sugarcane	Sugarcane	2.8	N/A	420	210
Turf	Turf	1.0	2600	N/A	1300

10.0 Data Needs and Label Requirements

10.1 Toxicology

No studies are required.

10.2 Residue Chemistry

- Additional method validation data using Method AM-0691B-0297-4; recovery data are needed for barley grain and straw at fortification levels of 6 and 15 ppm, respectively, and for wheat straw at 30 ppm. Additional method validation data using Method AM-0941-1094-0 are also needed for soybean seeds at a spike level of 10 ppm.

- Revise/improve Method II of PAM Vol. II to include an acid hydrolysis step and submit additional validation data. Method II should also be re-written specifically for the analysis of the parent dicamba and its metabolite 3.6-dichloro-2-hydroxybenzoic acid metabolite in animal matrices.

- Multiresidue methods recovery data for the dicamba metabolites of concern (5-OH dicamba and DCSA).

- Storage stability data for sugarcane molasses and animal commodities.

- Residue data and tolerances for soybean forage and hay if no feeding restrictions appear on the label.

- Magnitude of the residue data for sugarcane. In lieu of submitting additional data the registrants have the option of relying on the available/submitted data provided they revise their product labels for consistency with the reviewed data.

10.3 Occupational and Residential Exposure

No Data Required

References

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Hartge P, Colt JS, Severson RK, et al. 2005. Residential herbicide use and risk of non-Hodgkin's lymphoma. Cancer Epidemiology, Biomarkers and Prevention 14:934-7.

Hawkins, M.; Review of Dicamba Incident Reports; Chemical #029801; DP Barcode D316974; July 28, 2005.

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Olinger, C., **Dicamba:** Acute and Chronic Dietary Exposure Assessments for the Reregistration Eligibility - Phase 1; PC Code: 029801; DP Barcode: D317702; August 2005.

Olinger, C., **Dicamba:** Residue Chemistry Considerations for the Reregistration Eligibility Decision (RED) Document; PC Code: 029801; DP Barcode: D317703; August 2005.

Appendix A: Toxicology Assessment

Table A3. Data requirements (CFR 158.340) for Dicamba

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	Oral Subchronic (rodent)	yes	yes[1]
870.3150	Oral Subchronic (nonrodent)	yes	yes[1]
870.3200	21-Day Dermal	yes	yes
870.3250	90-Day Dermal	no	NA
870.3465	90-Day Inhalation	no	NA
870.3700a	Developmental Toxicity (rodent)	yes	yes
870.3700b	Developmental Toxicity (nonrodent)	yes	yes
870.3800	Reproduction	yes	yes
870.4100a	Chronic Toxicity (rodent)	yes	yes
870.4100b	Chronic Toxicity (nonrodent)	yes	yes
870.4200a	Oncogenicity (rat)	yes	yes
870.4200b	Oncogenicity (mouse)	yes	yes
870.4300	Chronic/Oncogenicity	yes	yes
870.5100	Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5375	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5xxx	Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a	Acute Delayed Neurotox. (hen)	no	no
870.6100b	90-Day Neurotoxicity (hen)	no	no
870.6200a	Acute Neurotox. Screening Battery (rat)	yes	yes
870.6200b	90 Day Neuro. Screening Battery (rat)	yes	yes
870.6300	Develop. Neuro	yes	yes
870.7485	General Metabolism	yes	yes
870.7600	Dermal Penetration	yes	yes
Special Studies for Ocular Effects			
	Acute Oral (rat)	no	no
	Subchronic Oral (rat)	no	no
	Six-month Oral (dog)	no	no

1. Requirements are satisfied by chronic oral toxicity studies.

Summaries of Carcinogenicity and Mutagenicity Studies

Carcinogenicity Study in Rats

Executive Summary: In a combined chronic toxicity/carcinogenicity study (MRID 00146150), groups of 60 male and 60 female CD rats were fed diets containing dicamba (86.8% a.i.; Lot no. 52625110) at 0, 50, 250 ro 2500 ppm for 115 (males) or 117 (females) weeks. These doses

correspond to 0, 2, 11 or 107 mg/kg bw/day for males and 0, 3, 13 or 127 mg/kg bw/day for females. Treatment had no adverse effect on survival, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, organ weights or gross pathology. Histopathology revealed increases in malignant lymphomas in males (0/60, 0/60, 4/60 and 4/60 at 0, 50, 250 and 2500 ppm, respectively) and thyroid parafollicular cell carcinomas in males (1/60, 0/60, 2/60 and 5/60 at 0, 50, 250 and 2500 ppm, respectively). The Cochran-Armitage trend test showed a statistically significant ($p \leq 0.05$) tendency for the proportion of animals with tumors to increase steadily with increase in dose. Pairwise comparison (Fisher's Exact test) showed no statistical significance. Therefore, these tumors were not considered to be toxicologically significant.

Under the conditions of this study, dicamba was not carcinogenic in male or female rats at the doses tested. The lack of systemic toxicity indicate that the animals may have tolerated higher doses (i.e., an MTD was not achieved). However, the doses employed in this study were approved by the Agency (Memo: S. April to R. Taylor, RD, dated 09/26/86).

Discussion of Tumor Data:
The administration of dicamba to rats up to 2500 ppm (107 mg/kg/day for males, 127 mg/kg/day for females) in the diet revealed increases in malignant lymphomas in males (0/60, 0/60, 4/60 and 4/60 at 0, 50, 250 and 2500 ppm, respectively) and thyroid parafollicular cell carcinomas in males (1/60, 0/60, 2/60 and 5/60 at 0, 50, 250 and 2500 ppm, respectively). The Cochran-Armitage trend test showed a statistically significant ($p \leq 0.05$) tendency for the proportion of animals with tumors to increase steadily with increase in dose. Pairwise comparison (Fisher's Exact test) showed no statistical significance. Therefore, these tumors were not considered to be toxicologically significant.

Adequacy of the Dose Levels Tested:

The Dose Adequacy Review Team (DART) reviewed the dosages of the study and concluded that the dose levels in the chronic toxicity/carcinogenicity study in rats could have been higher based on kinetics data which indicated that saturation of excretion occurred at a dose ranging from >200 to 400 mg/kg/day. However, retesting at a dose greater than 300 mg/kg/day, for example, would not be recommended based on the saturation data, which showed evidence of saturation of excretion at >200 mg/kg/day. Retesting at a dose of 300 mg/kg/day would not be expected to alter the conclusion that there was no carcinogenic effect. Since the doses in the rat carcinogenicity study (107/127 mg/kg/day) were within a factor of around two fold of the saturation point (>200-400 mg/kg/day), the doses were considered to be adequate for assessment of carcinogenicity. Therefore, the DART concluded that a new chronic toxicity/carcinogenicity study in the rat was not required (TXR No. 0053647).

Carcinogenicity Study in Mice

Executive Summary:
In a carcinogenicity study (MRID 40872401), groups of 52 male and 52 female CD-1 mice were fed diets containing dicamba (86.8% a.i.; Lot no. 52625110) at 0, 50, 150, 1000 or 3000 ppm for 89 (males) or 104 (females) weeks. These doses correspond to 0, 5.5, 17.2, 108 or 358 mg/kg

bw/day for males and 0, 5.8, 18.8, 121 or 354 mg/kg bw/day for females. Mortality was significantly increased in males at 150 ppm and at 3000 ppm; the cause of mortality was amyloidosis. The incidence of this lesion was higher than any other single factor among males that died in all groups especially the high dose. Except for a significant decrease at 150 ppm, survival among treated females was comparable to that of the controls. Body weight gain was higher in treated males than control males while there was a 17% decrease in body weight gain in females at 3000 ppm. No treatement-related effects were seen in food consumption, hematology, organ weights or gross pathology. Histopathology revealed a statistically significant ($p < 0.05$) increase in lymphosarcomas in females at 150 ppm only (8/52, 15%) compared to controls (2/52, 4%). The increase was not considered to be treatment-related due to lack of a dose-response and the incidences were within the historical control range (6-33%). Additionally, the incidence in the concurrent control (4%) was below the historical range.

Under the conditions of this study, dicamba was not carcinogenic in male or female mice at the doses tested. The lack of systemic toxicity indicate that the animals may have tolerated higher doses (i.e. and MTD was not achieved). However, the doses employed in this study were approved by the Agency (Memo: S. April to R. Taylor, RD, dated 11/15/84).

Discussion of Tumor Data:
The administration of dicamba to mice up to 3000 ppm (358 mg/kg/day for males, 354 mg/kg/day for females) in the diet revealed a statistically significant ($p < 0.05$) increase in lymphosarcomas in females at 150 ppm only (8/52, 15%) compared to controls (2/52, 4%). The increase was not considered to be treatment-related due to lack of a dose-response and the incidences were within the historical control range (6-33%). Additionally, the incidence in the concurrent control (4%) was below the historical range.

Adequacy of the Dose Levels Tested:

The DART revisited the 1995 decision by the RfD/Peer Review Committee that the mouse carcinogenicity study was not tested at a high enough doses to evaluate carcinogenicity in the mouse. The DART concluded that 3000 ppm is an adequate dose in the mouse cancer study and decided that a new mouse carcinogenicity study was not needed (TXR No. 0053647).

Mutagenicity

The RfD/Peer Review Committee reviewed the toxicology database of dicamba and determined that mutagenicity studies satisfied the minimum mutagenicity testing as per the pre-1991 guidelines (TXR No. 0012037, 7/29/96). Results are summarized as follow: negative for Ames (Salmonella), negative for WPU (E. Coli WP2), negative for SRL (sex-linked recessive lethal in Drosophila), negative for YE3 (S. cerevisiae mitotic recombination in strain D3), negative for UDH (UDS with WI-38 human lung fibroblasts), negative for SAR (differential toxicity with S. typhimurium), negative for chromosome aberration in the CHO cells; positive for REP (differential toxicity with E. Coli polA), positive for REW (differential toxicity with B. subtilis). Other published studies included positive UDS in cultured human lymphocytes w/S9, slight increase of SCE in cultured human lymphocytes with plus -minus activity; positive in an in vivo

assay for unwinding of liver DNA in i.p. injected rats (Environ Milec Mutagen 15: 131-135, 1990); negative for Salmonella and E. Coli WP2 (Mut. Res 116: 185-216, 1983); Negative for aberrations in rat bone marrow (Mut. Res 321:219-228, 1994).

Structure Activity Relationship Analysis for Carcinogenicity

The Structure Activity Relationship (SAR) showed that the concern level for carcinogenic potential is low. According to the OncoLogic Cancer Expert System, there is a Low-Moderate concern for para-dichlorobenzene but the substituents of dicamba lower the concern to Low. A structurally similar chemical, 2,4-D, is negative for carcinogenicity with a negative Ames test but positive chromosomal aberration and CHO tests. Other structurally similar chemicals, 5-chlorosalicylic acid, dichlorobenzoic acid, and chlorobenzoic acid have negative Ames tests, but no carcinogenicity data are available.

OTHER TOXICOLOGY STUDIES

Executive summaries for studies not described in the main body of the document are provided in the following pages.

In an acute neurotoxicity study (MRID 42774104) groups of Crl:CD BR rats (10/sex/dose) received a single oral (gavage) administration of dicamba (86.9%) in corn oil at doses of 0, 300, 600, or 1200 mg/kg. Vehicle controls received corn oil only. Positive controls received acrylamide at 50 mg/kg/day by intraperitoneal injection on seven consecutive days. At 300 mg/kg, transiently impaired respiration; rigidity upon handling, prodding or dropping; freezing of movement when touched; decreased arousal and fewer rears/minute compared to controls; impairment of gait and righting reflex were observed in both sexes. In addition, males showed decreased forelimb grip strength. With the exception of the decrease in forelimb grip strength, which persisted until day seven, these effects were observed only on the day of dosing. In addition, at 600 mg/kg, both sexes showed decreases in locomotor activity and males showed significant decreases in tail flick reflex and a raised posture when placed in an open field. These effects were also observed only on the day of dosing. At the highest dose level tested (1200 mg/kg), both males and females showed an impaired startle response to an auditory stimulus. The effect was significant in males on day seven and in females on the day of dosing. In addition, males showed decreases in body weight (5 - 9%), body weight gain (24%) and food consumption (13% between days 0 and 7). The LOAEL was 300 mg/kg based on the several neurologic signs listed above; a NOAEL was not established. The submitted study is classified as **acceptable/guideline** and satisfies the Guideline requirements for an acute neurotoxicity screening battery in rats.

Subchronic Neurotoxicity Study in the Rat

In a subchronic neurotoxicity study (MRID No. 43245210), Sprague-Dawley rats (10/sex/dose) were fed diets containing dicamba (86.9%) at 0, 3000, 6000, or 12000 ppm (0, 197.1, 401.4, 767.9 mg/kg/day for males and 0, 253.4, 472.0 or 1028.9 mg/kg/day for females, respectively) for 13 weeks. Neurobehavioral evaluations, consisting of FOB, locomotor activity, and auditory startle response, were conducted at prestudy and during Weeks 4, 8 and 13. No toxicologically

significant differences were noted in either the mean body weights or food consumption of the treated animals. Neurobehavioral evaluations at the 4-, 8-, and 13-week evaluations revealed abnormal FOB observations consisting of rigid body tone, slightly impaired righting reflex and impaired gait. At Week 13 the incidences of these findings were decreased. Rigid body tone was also noted during evaluation of the righting reflex and landing foot splay. The NOAEL was 401 mg/kg/day and the LOAEL was 768 mg/kg/day based on rigid body tone, slightly impaired righting reflex and impaired gait. The study is classified as **acceptable/guideline** and satisfies the guideline requirements (870.6200b) for a subchronic neurotoxicity study in the rat.

21/28-Day Dermal Toxicity – Rat (870.3200)

In a 28-day dermal toxicity study (MRID 45814501), Dicamba (91.0% a.i., batch #B2826511) was applied to the shaved skin of 10 male and 10 female Alpk:AP ,SD rats /sex/dose at dose levels of 0, 30, 300 or 1000 mg/kg bw/day, 6 hours/day for 5 days/week during a 28-day period.

Clinical observations, body weights and food consumption were measured throughout the study. Urine samples were taken for clinical pathology during week 4 of the study. A functional observational battery of all animals consisting of: detailed clinical observations, including quantitative assessments of landing foot splay, sensory perception and muscle weakness, and assessment of motor activity was performed on day 22. At the end of the scheduled period, the animals were killed and subjected to a post mortem examination. Blood samples were taken for clinical pathology, selected organs and specified tissues were taken for subsequent histopathological examination.

There were no changes indicative of systemic toxicity in either sex. There were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Histopathological changes indicative of irritation were seen in skin from the application site in both sexes given 1000 or 300 mg/kg/day and in some males given 30 mg/kg/day. **A LOAEL for systemic toxicity was not established. The NOAEL is 1000 mg/kg/day the highest dose tested.**

This 28-day dermal toxicity study in the rat is **acceptable/ guideline**, and satisfies the guideline requirement for a 28-day dermal toxicity study (OPPTS 870.3200 ; OECD 410) in the rat.

21/28-Day Dermal Toxicity – Rabbit (870.3200)

In a 21-day dermal study (MRID 40547901), New Zealand white rabbits (5/sex/group) received 15 repeated dermal applications of Dicamba in deionized water at dose levels of 0, 40, 200, or 1000 mg/kg/day , 6 hours/day, 5 days/week over a three week period. No systemic toxicity was observed at any dose level. Dose-related dermal irritation was observed at the application sites. Desquamation was seen predominantly in the 1000 mg/kg/day group while moderate erythema, moderate edema and atonia were observed exclusively in the 1000 mg/kg/day group. A dose-related incidence of fissuring was noted in the 200 and 1000 mg/kg/day groups. The severity of acanthosis and the incidence of hyperkeratosis was increased at these sites in rabbits at 200 and 1000 mg/kg. **For systemic toxicity, the NOEL was 1000 mg/kg/day (HDT); a systemic LOEL was not be established.**

This 28-day dermal toxicity study in the rat is **acceptable/ guideline**, and satisfies the guideline requirement for a 21-day dermal toxicity study (OPPTS 870.3200 ; OECD 410) in the rabbit.

Subchronic Oral Toxicity- Rat (870.3100)
In a 13-week subchronic toxicity study (MRID 44623101), dicamba technical (89.4% a.i.) was administered to HanIbm:WIST (Wistar) rats (10 or 20 rats/sex/dose) by feeding at dose levels of 0, 500, 3000, 6000, or 12,000 ppm (equivalent to 0/0, 40.1/43.2, 238.7/266.4, 479.4/535.6, or 1000.0/1065.3 mg/kg/day [M/F]) for 13 weeks. Following 13 weeks of treatment, 10 rats/sex/dose were sacrificed. Rats (10/sex) in the control and 12,000 ppm groups were maintained for a 4-week recovery period to determine the reversibility of effects.

No treatment-related deaths were observed in any treatment group. The liver was the target organ, as evidenced by microscopic liver changes associated with clinical serum chemistry changes and increased relative (to body) liver weights (↑20-23%) in both sexes at the high dose. The livers of the 12,000 ppm females exhibited slight centrolobular hepatocyte hypertrophy (4/10) and an increased incidence of minimal to moderate hepatocellular pigmentation (5/10). Both sexes exhibited increased alkaline phosphatase (↑62-76%), serum alanine aminotransferase (↑59-66%), and serum aspartate aminotransferase (↑29%) activities compared to the controls. Females exhibited an increase in mean gamma glutamyl transferase activity (↑136%) while males showed a decrease activity (↓50%) compared to the controls.

Other effects observed in the 12,000 ppm rats were transient hypothermia (weeks 1-4), reduced activity, slower movements, decreased food consumption, and less efficient food utilization than the controls throughout the treatment period. Lower mean final body weights (↓18-20%), body weight gains (↓28-40%) and adipose tissue content were observed compared to the controls. Decreases in protein (↓10-15%) and globulin (↓16-26%) levels were observed in both sexes. In females, decreased mean hemoglobin concentration (↓4%) and red blood cell counts (↓4%), and decreased mean corpuscular hemoglobin concentration (↓3%) were observed. Significant ($p<0.05$ or $p<0.01$) increases of white blood cell count (↑13%) and lymphocyte count (↑33%) were observed in 12000 ppm females compared to the controls. Males had a lower mean platelet count (↓7%) and shorter partial thromboplastin time (↓11%) compared to the controls. Urinalysis showed that males excreted more triple phosphate crystals in the 12000 ppm group, whereas females excreted more uric acid crystals in the 12000 and 6000 ppm groups at week 12. Following a 4-week recovery period, all observed effects were recovered.

The LOAEL for this study is 12,000 ppm (1000 mg/kg/day), based on clinical signs, reduced body weight gains, hematological and clinical serum chemistry changes in both sexes, centrolobular hepatocyte hypertrophy and hepatocellular pigmentation in females, and increased relative (to body) liver weights for both sexes. The NOAEL is 6000 ppm (479 mg/kg/day).

This 13-week subchronic toxicity study is classified **acceptable/guideline (870.3100)** and satisfies the guideline requirement for a subchronic toxicity study in rodents.

Chronic Toxicity - Dog (870.4100b)

In a chronic oral toxicity study (MRID 40321102), dicamba (86.8, a.i., lot # 52625110) was administered to beagle dogs (4/sex/group) in diet at dose levels of 0, 100, 500, or 2500 ppm (0, 2, 11, or 52 mg/kg/day, respectively) for one year.

The investiagated parameters in this study, which included behavior, mortality, body weight, food consumption, hematology, serum chemistry, urinalysis as well as macroscopic and histologic examination of tissues, did not reveal any apparent adverse effect from the test compound. Therefore, the NOAEL for dicamba was 2500 ppm in the diet (about 52 mg/kg/day), the highest dosage administered in this test; the absence of any adverse effects among treated animals indicated that the MTD was not attained.

This one-year dog study is classified **Acceptable/Guideline** and satisfies the guideline requirement for a chronic toxicity study in dogs.

Metabolism - Rat (870.7485)

In a plasma kinetics study, (MRID 44609801), [phenyl-U-^{14}C]- dicamba ([^{14}C]-dicamba; 86.0% a.i. radiochemical purity), was administered as a dietary admix to 4 male and 4 female Wistar and Sprague-Dawley at 900, 1500, 3000, 4500, and 12000 ppm (Wistar rats) and 900, 1500, 3000, 6000 and 9000 ppm (Sprague-Dawley rats) for fourteen days, followed by a radioactive dose of 90, 150, 300, 450 mg/kg bw (Wistar rats) and 75, 125, 250, 500 and 800 mg/kg bw by a single gavage dose (in 10 ml/kg body weight 0.5% Tylose CB 30.000 in aqua bidest). Plasma levels were measured at various time intervals following radioactive dose.

A preliminary study in Wistar rats suggests excessive toxicity following repeated gavage doses. Therefore, the main study in both strains of rats was conducted as a dietary ad mix followed by a gavage dose of radiolabeled dicamba. In both strains of rats, the plasma levels reached a maximum level after 0.5-1 hour following the gavage dose and declined thereafter. The $AUC_{0-\infty}$ values were calculated from the plasma concentrations versus time curves at the respective dose levels indicated linear relationship with increase in dose up to a certain dose levels in both strains of rats indicating saturation of excretion. Initial plasma half-life was increased with increasing dose, but terminal half-life remains more or less constant in both strains of rats indicating saturation of excretion. Plasma half-life was increased with increasing dose giving no indication of saturation of oral absorption.

In Wistar rats, the increase in plasma AUC was linear with dose up to a level of 150 mg/kg bw in males and 300 mg/kg bw in females. Above these dose levels, plasma AUC-values increased more than dose. Sprague-Dawley rats showed similar results, with the increase in AUC being linear with dose up to a level of 125 and 250 mg/kg bw in males and females, respectively. Above these dose levels, plasma AUC-values increased more than dose. Considering that oral absorption was not saturated and that initial plasma levels went up with dose, the disproportionate increase in plasma AUC is clearly due to saturation of renal excretion of dicamba resulting in a longer plasma half-life. This is supported by half-life data in both species which showed an increase in plasma half-life with dose.

This plasma kinetics study in the rats is classified **Acceptable/Nonguideline (§85-1).**

Metabolism - Rat (870.7485)

In a plasma pharmacokinetic study (MRID 46022302), five groups of 4 male and 4 female Wistar rats received diets containing the equivalent of 50, 100, 200, 400, or 800 mg/kg dicamba/day for 90 days (Lot No. 52103810, 87.2% a.i.). On study days 29, 63, and 91, dietary supplementation of dicamba was stopped and rats in each group received an equivalent gavage dose of ^{14}C-dicamba (Lot No. 787-0102, >99% a.i., universally labeled in the phenyl group). Blood samples were drawn 0.5, 1, 2, 4, 6, 8, 12, 24, and 48 hours after treatment and the plasma radioactivity determined.

Absorption of the radiolabeled test material was rapid, with peak plasma concentrations found within 2 hours of treatment. Absorption was not saturated, even at the highest dose, as indicated by increasing plasma concentrations with dose. However, the increase in plasma concentration was disproportionate from dose as shown by the ≥ 2-fold increase in AUC from one dose group to the next at doses >100 mg/kg. Elimination of radiolabel from the plasma was tri-phasic, with the terminal-phase consistent between doses. However, the initial elimination phase increased with dose, particularly in the 400 and 800 mg/kg dose groups and is consistent with excretion saturation. No significant treatment-related differences between the sexes or time of radiolabel administration were found.

This plasma pharmacokinetic study in the rat is classified **Acceptable/Nonguideline** and satisfies its intent.

Metabolism - Rat (870.7485)

In a pharmacokinetic study (MRID 46022303), two groups of 3 male Wistar rats were given a single 200 mg/kg gavage dose of ^{14}C-dicamba (Lot No. 787-0102, >99% a.i., universally labeled in the phenyl group). One group of rats was pretreated with a 150 mg/kg IP dose of probenecid , a known competitive inhibitor of renal anion transport, 30 minutes prior to dicamba dosing. Blood samples were drawn 0.5, 1, 2, 4, 6, 8, 12, 24, and 48 hours after gavage treatment and the plasma radioactivity determined.

The time to peak plasma concentration in rats treated with ^{14}C-dicamba occurred within 0.5 hours while peak plasma concentration was reached at 1.0 hour in the probenecid/dicamba rats. However, pretreatment with probenecid increased plasma AUC by a factor of 1.54. Although the terminal phase of elimination remained relatively the same, the initial and intermediate elimination phases were increased by a factor of two. These data suggest that both dicamba and probenecid, act as inhibitors of renal anion transport.

This pharmacokinetic study in the rat (MRID 46022303) is classified **Acceptable/Nonguideline** and satisfies its intent.

Appendix B: Use Profile

Table B.1 Dicamba Use Profile (8/2/2005)			
Use Sites	Forms[1]	Max Application Rate (Unit/Area)	Max Application Rate (year)
Non-Food/Non-Feed Uses			
Agricultural Fallow/Idleland (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Agricultural rights-of-way/fencerows/hedgerows (Non-crop)[2]	Dimethylamine Salt, Sodium Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A)
		7.7 (lbs a.e./A)	7.7 (lbs a.e./A)
Agricultural Uncultivated Areas (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Agricultural/Farm Structures/Buildings and Equipment (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Airports/Landing Fields (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Commercial/Industrial Lawns (Non-crop)	Dimethylamine Salt	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Commercial/Institutional/ Industrial Premises/Equipment (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Drainage Systems (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Fencerows/Hedgerows (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Forest Plantings (reforestation programs)(tree farms, tree plantations, etc) (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Forest Trees (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Golf Course Turf	Dimethylamine Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.e./A) year
Household Domestic Dwellings (Non-crop)	Dimethylamine Salt	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Industrial Areas (Outdoor) (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Nonagricultural Outdoor Buildings/Structures (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year

Table B.1 Dicamba Use Profile (8/2/2005)			
Use Sites	Forms[1]	Max Application Rate (Unit/Area)	Max Application Rate (year)
Nonagricultural Rights-of-way/Fencerows/ Hedgerows (Non-crop)	Dimethylamine Salt, Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Nonagricultural Uncultivated Area/Soils (Non-crop)	Dimethylamine Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Ornamental Lawns and Turf	Dimethylamine Salt, Sodium Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.i../A) year
Ornamental Sod Farm	Dimethylamine Salt, DGA	1.0 (lbs a.e./A)	1.0 (lbs a.e./A) year
Paths/Patios (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e/A)	2.0 (lbs a.e./A) year
Paved Areas (Private Roads/Sidewalks (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e/A)	2.0 (lbs a.e./A) year
Recreation Area Lawns	Dimethylamine Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Recreational Areas	Dimethylamine Salt, DGA	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Residential Lawns	Dimethylamine Salt	1.0 (lbs a.i./A)	1.0 (lbs a.i./A) year
Urban Areas (Non-crop)	Dimethylamine Salt	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Food/Feed Uses			
Agricultural Crops/Soils	Dimethylamine Salt, Sodium Salt	2.0 (lbs a.e/A)	2.0 (lbs a.e./A) year
Agricultural Fallow/Idleland	All	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
Agricultural/Farm Premises	Dimethylamine Salt, DGA	1.0 (lbs a.e./A)	1.0 (lbs a.e./A) year
Agricultural/Farm Structures/Buildings and Equipment	Dimethylamine Salt	1.0 (lbs a.e./A)	1.0 (lbs a.e./A) year
Asparagus	Dimethylamine Salt, Sodium Salt, DGA	0.5 (lbs a.e./A)	0.5 (lbs a.e./A) year
Barley	Dimethylamine Salt, Sodium Salt, DGA, IPA	0.25 (lbs a.e./A)	0.38 (lbs a.e./A) year
Corn (field, pop, seed, silage)	Dimethylamine Salt, Sodium Salt, DGA, Potassium Salt	0.5 (lbs a.e./A)	0.75 (lbs a.e./A) year
Cotton	Dimethylamine Salt, DGA	0.25 (lbs a.e./A)	2.0 (lbs a.e./A)
Hay	Dimethylamine Salt, Sodium Salt, DGA	2.0[3] (lbs a.e./A)	2.0 (lbs a.e./A) year
Millet (Proso)	Dimethylamine Salt	0.125 (lbs a.e/A)	0.125 (lbs a.e./A) year

Table B.1 Dicamba Use Profile (8/2/2005)			
Use Sites	Forms[1]	Max Application Rate (Unit/Area)	Max Application Rate (year)
Oats	Dimethylamine Salt, Sodium Salt, DGA	0.125 (lbs a.e./A)	1.0 (lbs a.e/A) year
Pastures[4]	Dimethylamine Salt, Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
		7.7 (lbs a.e/A)	7.7 (lbs a.e/A) year
Rangeland[5]	Dimethylamine Salt, Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e./A) year
		7.7 (lbs a.e./A	7.7 (lbs a.e/A) year
Rye	Dimethylamine Salt	0.5 (lbs a.e./A)	1.0 (lbs a.e./A) year
Sorghum	All	.2748 (lbs a.e./A)	0.5 (lbs a.e./A) year
Soybean	Sodium Salt, DGA	2.0 (lbs a.e./A)	2.0 (lbs a.e/A) year
Sudangrass	Dimethylamine Salt	0.5 (lbs a.e./A) As listed for Hay.	1.0 (lbs a.e./A) year
Sugarcane	Dimethylamine Salt, Sodium Salt, DGA	2.8 (lbs a.e./A)	2.8 (lbs a.e./A) year
Wheat	Dimethylamine Salt, Sodium Salt, DGA, IPA	0.5 (lbs a.e./A)	1.0 (lbs a.e./A) year

1. There are 5 forms of dicamba used in this Master Label: Dimethylamine Salt (PC Code 29802), Sodium Salt (PC Code 29806), Diglycoamine [DGA] (PC Code 128931), Isopropylamine Salt [IPA] (PC Code 128944), and Potassium Salt (PC Code 129043)

2. Label 100-884 list 7.7 lbs a.e./A as the maximum rate for spot treatment for Agricultural right-of-way uses. The 2.0 lbs a.e./ A is what the registrant stated at the SMART Meeting as the rate they intended to support.

3. Based on label 51036-289 and 7969-131

4. Label 100-884 list 7.7 lbs a.e./A as the maximum rate for spot treatment for pasture uses. The 2.0 lbs a.e./ A is what the registrant stated at the SMART Meeting as the rate they intended to support.

5. Label 100-884 list 7.7 lbs a.e./A as the maximum rate for spot treatment for rangeland uses. The 2.0 lbs a.e./ A is what the registrant stated at the SMART Meeting as the rate they intended to support.

Appendix C: TOLERANCE REASSESSMENT SUMMARY

The established tolerances for dicamba are listed in 40 CFR §180.227. There are three dicamba tolerance expressions. Under 40 CFR §180.227 (a)(1), the tolerances are expressed in terms of the combined residues of the herbicide dicamba (3,6-dichloro-o-anisic acid) and its metabolite 3,6-dichloro-5-hydroxy-o-anisic acid. The tolerances listed in 40 CFR §180.227 (a)(2) are expressed in terms of the combined residues of dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid. Finally, the tolerances listed in 40 CFR §180.227 (a)(3) are expressed in terms of the combined residues of dicamba and its metabolites 3,6-dichloro-5-hydroxy-o-anisic acid and 3,6-dichloro-2-hydroxybenzoic acid.

The results of plant and animal metabolism studies suggest that the various tolerance expressions for dicamba are appropriate. The results of a confined rotational crop study indicate that tolerances need not be established for rotational crops pending label revisions to specify appropriate rotational crop restrictions.

A summary of the tolerance reassessment and recommended modifications in commodity definitions for dicamba is presented in Table C1.

Tolerances Established Under CFR §180.227 (a)(1)

Pending label revisions and/or adjustment of tolerances, there are adequate residue data to reassess the tolerances for: barley, grain, hay, and straw; corn, field, grain, forage, and stover; grass forage and hay; wheat grain, straw, forage and hay; and sorghum grain, forage, and stover.

The submitted data for many commodities do not support the established tolerances because they do not reflect the maximum use rates listed in Dicamba Master Use Profile. To fulfill reregistration requirements, the registrant are required to submit additional data for sugarcane. In lieu of submitting additional data, the registrants are given the option to rely on the available data provided they revise their product labels for consistency with the reviewed data.

HED will allow the translation of available/requested data from some crop commodities to agronomically related commodities with identical uses. Where this situation exists, any HED recommendations with regards to label revision and tolerance reassessment should apply to both crop commodities. The following translations have been made in this Residue Chemistry Chapter: (i) data from field corn grain and stover may be translated to pop corn grain and stover; (ii) data from wheat grain may be translated to proso millet grain and rye grain; (iii) data from wheat forage, hay, and straw may be translated to oat forage, hay, and straw; and (iv) data from wheat straw may be translated to proso millet straw

Pending submission of supporting storage stability data, an acceptable sugarcane processing study is available to reassess the established tolerance for sugarcane molasses. When the maximum HAFT combined residue level (0.183 ppm) of the RAC is multiplied by the observed concentration factor for sugarcane molasses (24.4x), the resulting level is 4.465 ppm which is higher than the current tolerance of 2.0 ppm. Based on these data, HED recommends that the tolerance for sugarcane molasses be increased from 2.0 ppm to 5.0 ppm, toxicological

considerations permitting.

The Agency no longer considers sugarcane forage and fodder to be significant livestock feed items, and these items have been deleted from Table 1 of OPPTS 860.1000. Therefore, the respective tolerances should be revoked.

The generic "corn, forage" tolerance should be revoked since a separate tolerance for field corn forage is established. The generic "corn, stover" tolerance should be revoked since separate tolerances are established for field corn stover and pop corn stover. The generic "corn, grain" tolerance should be split into: "corn, field, grain" and "corn, pop, grain".

Tolerances Needed Under CFR §180.227 (a)(1)

Tolerances are needed for proso millet forage and hay. The available/requested data for wheat forage and hay may be translated to proso millet forage and hay.

Tolerances are needed for rye grain, forage, and straw. The available/requested data for wheat grain, forage, and straw may be translated to rye grain, forage, and straw.

Tolerances Established Under CFR §180.227 (a)(2)

Pending label revisions and/or adjustment of tolerance, there are adequate data to reassess the established tolerance for asparagus.

A ruminant feeding study conducted at a dosing level of 1000 ppm is under review. Assuming this study is adequate sufficient data are available to reassess the established ruminant tolerances.

Tolerances Established Under CFR §180.227 (a)(3)

There are adequate data to reassess the tolerances for soybean seed and soybean hulls.

An acceptable soybean processing study is available to reassess the established tolerance for soybean hulls. When the HAFT combined residue level (7.44 ppm) for the RAC is multiplied by the observed concentration factor for soybean hulls (3.8x), the resulting level is 28.272 ppm which suggests that the existing tolerance of 13.0 ppm needs an upward adjustment. Based on these data, HED recommends that the tolerance for soybean hulls be increased from 13.0 ppm to 30.0 ppm.

There are adequate residue data on the aspirated grain fractions of sorghum, soybean, and wheat and may be translated to corn.

Tolerances That May Be Needed Under CFR §180.227 (a)(3)

It is the current Agency policy to allow label restrictions on the feeding/grazing of livestock animals on soybean forage and hay, thus, precluding the need for residue data and tolerances for these soybean commodities. HED defers to RD for verifying whether such restrictions exist on

product labels. If such restrictions appear on the labels, then residue data and tolerances for soybean forage and hay are not necessary. If no such restrictions appear on the labels, then the registrants are required to propose tolerances for soybean forage and hay; based on the available data, a tolerance level of 0.1 ppm would be appropriate for each soybean commodity. Concomitant with these tolerance proposals, the registrants are required to propose a maximum seasonal rate of 0.5 lb ae/A for preplant application on soybean grown for forage and hay only.

Pending Tolerance Petition:

PP#6E06209: Interregional Research Project No. 4 (IR-4) has submitted a petition, on behalf of the Agricultural Experiment Stations of MN, ND and WI, proposing the following permanent tolerances for the combined residues of the herbicide dicamba and its 5-hydroxy (5-OH) metabolite (3,6-dichloro–5-hydroxy-o-anisic acid) in/on: sweet corn forage at 1.0 ppm, fresh sweet corn at 0.1 ppm, and sweet corn stover at 1.0 ppm. HED's evaluation of residue data and analytical methods (DP Barcode D275611, 7/26/2001, G. Kramer) concluded that additional field residue trials need to be conducted and a revised Section F must be submitted before a favorable recommendation can be made.

Codex/International Harmonization

No Codex MRLs have been established for dicamba; therefore, issues of compatibility between Codex MRLs and U.S. tolerances do not exist. Compatibility cannot be achieved with the Canadian negligible residue limits or with Mexican MRLs because these levels are expressed in terms of parent compound only.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Dicamba Tolerances Listed Under 40 CFR §180.227 (a)(1) [Expressed in terms of the combined residues of dicamba and its metabolite 3,6-dichloro-5-hydroxy-*o*-anisic acid]			
Barley, grain	6.0	6.0	
Barley, hay	2.0	2.0	
Barley, straw	15.0	15.0	
Corn, field, forage	3.0	3.0	The combined residues ranged from <0.01 to 2.27 ppm in/on field corn forage harvested 39-71 days following the last of three sequential treatments for a total of 2.75 lb ae/A. The combined residues ranged from <0.01 to 2.45 ppm in/on field corn fodder harvested 66-123 days following same sequential treatments.
Corn, field, stover	3.0	3.0	
Corn, forage	0.5	Revoke	The generic "corn, forage" tolerance should be revoked since a separate tolerance for field corn forage is established.
Corn, grain	0.5	0.1	The combined residues ranged from <0.01 to 0.015 ppm in/on field corn grain samples harvested 69-123 days following the last of three sequential treatments for a total of 2.75 lb ae/A. The generic "corn, grain" tolerance should be split into: "corn, field, grain"; and "corn, pop, grain".
Corn, pop, stover,	3.0	3.0	HED will allow the translation of available data for field corn stover to pop corn stover. Any label revision for field corn should also be made for pop corn. Concurrently, any adjustment to the field corn stover tolerance should also be applied as necessary to the pop corn stover tolerance.
Corn, stover	0.5	Revoke	The generic "corn, stover" tolerance should be revoked since separate tolerances are established for field corn stover and pop corn stover.
Cotton, undelinted seed	5.0	TBD	
Cotton, meal	5.0	TBD	

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Crop Group 17 (grass forage, fodder, and hay)			The combined residues ranged 66-358 ppm in/on grass forage samples harvested immediately (0-day) following a single application at 2.0 lb ae/A (1x). The combined residues ranged 25-201 ppm in/on grass hay samples harvested 7 days following a single application 1x. Based on these data, HED is reassessing the grass forage tolerance at 400 ppm and the grass hay tolerance at 250 ppm. Concomitant with the reassessment of these tolerances, HED is requesting RD to verify that all dicamba labels specify a 0-day PHI/PGI for grass forage and a 7-day PHI for grass hay when applied at a maximum of 2.0 lb ae/A.
- Grass forage	125.0	400	
- Grass hay	200.0	250	
Millet, proso, grain	0.5	2.0	HED will allow the translation of available/requested data for wheat grain and straw to proso millet grain and straw since the Dicamba Master Use Profile indicates that the application rate of the two crops is identical. Any label revision for wheat should also be made for proso millet. Concurrently, any adjustment to the wheat grain and straw tolerances should also be applied as necessary to the proso millet grain and straw tolerances.
Millet, proso, straw	0.5	TBD	
Oat, grain	0.5	2.0	HED will allow the translation of available/requested data for wheat grain to oat grain since the Dicamba Master Use Profile indicates that the application rate of the two crops is identical.
Oat, forage	80.0	2.0	HED will allow the translation of available/requested data for wheat forage, hay, and straw to oat forage, hay, and straw since the Dicamba Master Use Profile indicates that the application rate of the two crops is identical.
Oat, hay	20.0	TBD	
Oat, straw	0.5	30	
Sorghum, grain	3.0	4.0	The maximum combined residues were 2.73 ppm (MRID 43245203) and 3.164 ppm (MRID 44089306) in/on sorghum grain harvested 30-42 days following sequential treatments for a total rate of 0.5 lb ae/A (1x the maximum rate listed in the Dicamba Master Use Profile). These data suggest that the established tolerance for sorghum grain may be too low. Based on the reviewed data, HED is recommending a tolerance level of 4.0 ppm for sorghum grain concomitant with label revision to specify a 30-day PHI.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	*Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Sorghum, forage	3.0	0.5	The maximum combined residues were 0.46 ppm (MRID 43245203) and 0.350 ppm (MRID 44089306) in/on sorghum forage samples harvested 20-72 days following a single postemergence application at 0.25 lb ae/A (0.5x the seasonal rate listed in the Dicamba Master Use Profile). The maximum combined residues were 8.22 ppm (MRID 43245203) and 4.29 ppm (MRID 44089306) in/on sorghum fodder (stover) samples collected at PHIs of 30-42 days following the last of two applications for a total rate of 0.5 lb ae/A (1x). These data suggest that the established tolerance for sorghum forage may be too high and the tolerance for fodder too low. Based on these data, HED is recommending tolerance levels of 0.5 ppm for sorghum forage and 10.0 ppm for sorghum stover concomitant with the following recommended label revisions: (i) a 20-day PHI and a maximum single/seasonal rate of 0.25 lb ae/A for sorghum forage; and (ii) a 30-day PHI for sorghum fodder (stover) at a maximum seasonal rate of 0.5 lb ae/A.
Sorghum, grain, stover	3.0	10	
Sugarcane, cane	0.1	TBD[1]	The available data do not support the maximum seasonal single/yearly rate of 2.8 lb ae/A that is listed in the Dicamba Master Use Profile because the sugarcane trials were conducted at an application rate of 2.0 lb ae/A. The maximum combined residues were 0.202 ppm in/on sugarcane harvested 87-173 days following a single layby application at 2.0 lb ae/A. The registrants are required to submit additional data on sugarcane reflecting a maximum single/yearly rate of 2.8 lb ae/A. Alternatively, the registrants may rely on the available data provided they are willing to revise their product labels for consistency with the reviewed data. If the registrants elect to choose the latter option, then they will be required to revise product labels to specify a maximum seasonal rate of 2.0 lb ae/A and an 87-day PHI for sugarcane. Based on the reviewed data, the existing tolerance of 0.1 ppm for sugarcane is too low, and HED is recommending that it be reassessed at 0.3 ppm *if* the registrants elect to revise product labels as detailed above.
Sugarcane, fodder	0.1	Revoke	These items are no longer regulated and have been removed from Table 1 of OPPTS 860.1000.
Sugarcane, forage	0.1	Revoke	

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Sugarcane, molasses	2.0	5.0	When the maximum HAFT combined residue level (0.183 ppm) of the RAC is multiplied by the observed concentration factor for sugarcane molasses (24.4x), the resulting level is 4.465 ppm which is higher than the current tolerance of 2.0 ppm. Based on these data, HED recommends that the tolerance for sugarcane molasses be increased from 2.0 ppm to 5.0 ppm, pending submission of supporting storage stability data.
Wheat, forage	80.0	TBD	Additional data are currently under review.
Wheat, grain	2.0	2.0	The combined residues were <0.01 to 0.15 ppm in/on samples of wheat grain harvested 63-125 days following one spring broadcast application at 0.25 lb ae/A. The combined residues were 0.039 to 1.4 ppm in/on grain samples harvested 6-12 days following the last of two treatments for a total of 0.5 lb ae/A.
Wheat, hay	20.0	TBD	Additional data are currently under review.
Wheat, straw	30.0	30.0	The combined residues were 0.011 to 0.97 ppm in/on samples of wheat straw harvested 63-125 days following one spring broadcast application at 0.25 lb ae/A. The combined residues were 0.13 to 26 ppm in/on straw samples harvested 6-12 days following the last of two treatments for a total of 0.5 lb ae/A.
Dicamba Tolerances Needed Under 40 CFR §180.227(a)(1)			
Millet, proso, forage	None	TBD	HED will allow the translation of available/requested data for wheat forage and hay to proso millet forage and hay since the Dicamba Master Use Profile indicates that the application rate for wheat is slightly higher than millet.
Millet, proso, hay	None	TBD	
Rye, grain	None	2.0	HED will allow the translation of available/requested data for wheat grain, forage, and straw to rye grain, forage, and straw since the Dicamba Master Use Profile indicates that the yearly application rate of the two crops is identical.
Rye, forage	None	TBD	
Rye, straw	None	30.0	
Dicamba Tolerances Listed in 40 CFR §180.227 (a)(2) [Expressed in terms of the combined residues of dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid]			
Asparagus	4.0	4.0	Th combined residues ranged 0.28-3.29 ppm in/on asparagus samples harvested 24 hours following a single application at 1x the maximum rate listed in the Dicamba Master Use Profile. These data support the currently established tolerance of 4.0 ppm on asparagus pending verification by RD that the label PHI for asparagus is 24 hours or 1 day.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Cattle, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Cattle, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Cattle, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Cattle, meat byproducts	0.2	3.0	*Cattle, meat by-products, except kidney.* Reassessed values are based on a new ruminant feeding study currently under review.
Cattle, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Goat, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Goat, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Goat, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Goat, meat byproducts	0.2	3.0	*Goat, meat by-products, except kidney*
Goat, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Hog, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Hog, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Hog, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Hog, meat byproducts	0.2	3.0	*Hog, meat by-products, except kidney*
Hog, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Horse, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Horse, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Horse, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Horse, meat byproducts	0.2	3.0	*Horse, meat by-products, except kidney* Reassessed values are based on a new ruminant feeding study currently under review.
Horse, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Milk	0.3	0.2	Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, fat	0.2	0.3	Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, kidney	1.5	25	Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, liver	1.5	Revoke	Residues in liver will be covered by redefined meat by-products tolerance.
Sheep, meat byproducts	0.2	3.0	*Sheep, meat by-products, except kidney* Reassessed values are based on a new ruminant feeding study currently under review.
Sheep, meat	0.2	0.25	Reassessed values are based on a new ruminant feeding study currently under review.
Dicamba Tolerances Under 40 CFR §180.227(a)(3) [Expressed in terms of the combined residues of dicamba and its metabolites 3,6-dichloro-5-hydroxy-*o*-anisic acid and 3,6-dichloro-2-hydroxybenzoic acid]			
Grain, aspirated grain fractions	5100	1000	There are adequate residue data on the aspirated grain fractions of sorghum, soybean, and wheat, and can be translated to corn.
Soybean, hulls	13.0	30.0	When the maximum HAFT combined residue level (7.44 ppm) of the RAC is multiplied by the observed concentration factor for soybean hulls (3.8x), the resulting level is 28.272 ppm which suggests that the existing tolerance of 13.0 ppm is too low. HED recommends that the tolerance for soybean hulls be increased from 13.0 ppm to 30.0 ppm.
Soybean, seed	10.0	10.0	The highest total residues were 8.13 ppm in/on samples of soybean seed harvested 6-8 days following treatments at 1.25x the maximum rate listed in the Dicamba Master Use Profile.

Table 9. Tolerance Reassessment Summary for Dicamba.			
Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments/ *Correct commodity definition*
Dicamba Tolerances That May Be Needed Under 40 CFR §180.227(a)(3)			
Soybean, forage	None	TBD	It is the current Agency policy to allow label restrictions on the feeding/grazing of livestock animals on soybean forage and hay, thus, precluding the need for residue data and tolerances. HED defers to RD for verifying whether such restrictions exist on product labels. If such restrictions appear on the labels, then residue data and tolerances for soybean forage and hay are not necessary. If no such restrictions appear on the labels, then the registrants are required to propose tolerances for soybean forage and hay; based on the available data, a tolerance level of 0.1 ppm would be appropriate for each soybean commodity. Concomitant with these tolerance proposals, the registrants are required to propose a maximum seasonal rate of 0.5 lb ae/A for preplant application on soybean grown for forage and hay.
Soybean, hay	None	TBD	

[1] TBD = To be determined. Additional data/information are required for tolerance reassessment.

13544

R115338

Chemical:	**Dicamba**
PC Code:	**029801**
HED File Code	**14000 Risk Reviews**
Memo Date:	**09/13/2005**
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